

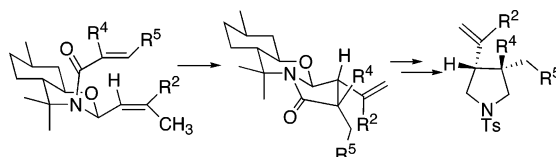
Diastereoselective Intramolecular Alder–Ene Reaction on Chiral Perhydro-1,3-benzoxazines. A Rapid Entry to Enantiopure *cis*-3,4-Disubstituted Pyrrolidines

Rafael Pedrosa,* Celia Andrés,* Laura Martín, Javier Nieto, and Carlos Rosón

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Valladolid, Dr. Mergelina s/n, 47011 Valladolid, Spain

pedrosa@qo.uva.es

Received February 26, 2005



Chiral 3-acryloyl-2-vinyl-substituted 1,3-perhydrobenzoxazines derived from (–)-8-aminomenthol participate in an ene reaction leading to 3,4-disubstituted pyrrolidinone derivatives with excellent diastereoselectivity. The cycloadducts were transformed into enantiopure 3,4-disubstituted pyrrolidines after elimination of the chiral adjuvant.

Introduction

The ene reaction¹ represents one of the most important and versatile bond-forming reactions in organic chemistry owing to a great variety of suitable starting substrates. Ene reactions involving alkenes² (olefin–ene or Alder–ene reaction), carbonyl functionalities³ (carbonyl–ene reaction), azo compounds,⁴ singlet oxygen,⁵ nitroso groups,⁶ or phosphorus derivatives⁷ as enophiles have been used in carbon–carbon and carbon–heteroatom transformations with olefins. Reactions involving hetero–ene components such as enoles⁸ and enamines⁹ are also known. The use of the ene reaction for synthetic purposes is often limited due to its high activation energy, particularly in olefin– and carbonyl–ene reactions. High temperatures

are generally required, although reactions catalyzed by Lewis acids proceed under mild conditions and often with improved stereoselectivity.

The intramolecular ene reaction¹⁰ generally takes place more easily than the corresponding intermolecular reaction due to the less negative entropy activation, and generally occurs with high regio- and stereocontrol depending on the tether connecting the ene and enophile components.

The absolute stereochemistry of the final products can be controlled by preexisting stereogenic centers¹¹ or chiral Lewis acids as promoters,¹² but the use of chiral auxiliaries as controllers of chirality has not been studied enough.¹³

Recently, we have shown that chiral perhydro-1,3-benzoxazines derived from (–)-8-aminomenthol constitute useful chiral auxiliaries in thermally induced keto–ene cyclizations,¹⁴ and during our studies in intramolecular Diels–Alder reaction of styrene derivatives, we found that 2-(*trans*-1-methyl-2-phenylethenyl)perhydro-1,3-benzoxazine derivative **5d** was easily transformed by

* To whom correspondence should be addressed. Fax: Int + 983 423 013.

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(2) Snider, B. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, p 1.

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(4) For a review on imino–ene reactions, see: Borzilleri, R. H.; Weinreb, S. M. *Synthesis* **1995**, 347.

(5) (a) Stratakis, M.; Orfanopoulos, M. *Tetrahedron* **2000**, *56*, 1595.

(b) Prein, M.; Adam, W. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 477.

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(11) See, for example: (a) Helmboldt, H.; Rehbein, J.; Hiersemann, M. *Tetrahedron Lett.* **2004**, *45*, 289. (b) Alcaide, B.; Almendros, P.; Pardo, C.; Rodríguez-Ranera, C.; Rodríguez-Vicente, A. *J. Org. Chem.* **2003**, *68*, 3106. (c) Watanabe, B.; Yamamoto, S.; Sasaki, K.; Nakagawa, Y.; Miyagawa, H. *Tetrahedron Lett.* **2004**, *45*, 2767. (d) Noguchi, M.; Matsushita, R.; Takamura, S.; Uchida, T.; Takehiko, U.; Kakehi, A.; Shiro, M.; Yamamoto, H. *Tetrahedron Lett.* **2000**, *41*, 8489. (e) Nayak, S. K.; Thijs, L.; Zwanenburg, B. *Synlett* **1998**, 1187. (f) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949.

thermolysis into the ene cyclization product **6d** instead of the expected tetrahydrobenz[*f*]isoindoline derivative cyloadduct.¹⁵

We present now a full account on the behavior of 3-acryloyl-2-vinylperhydro-1,3-benzoxazines derived from (–)-8-aminomenthol¹⁶ in intramolecular Alder–ene reactions and their use in preparation of enantiopure *cis*-3,4-disubstituted pyrrolidines.¹⁷ This heterocycle is known to constitute major frameworks of alkaloids which display important biological activity.¹⁸ Nevertheless, general and effective methods for the synthesis of enantioselective *cis*-3,4-disubstituted pyrrolidines are noticeably rare.¹⁹

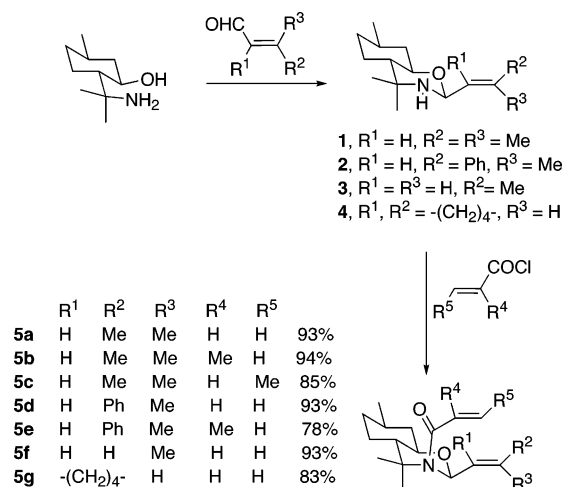
Results and Discussion

The starting chiral perhydro-1,3-benzoxazines **5a–g** were prepared in two steps as single diastereomers and in good chemical yields, as summarized in Scheme 1. Condensation of (–)-8-aminomenthol with α,β -unsaturated aldehydes in CH_2Cl_2 at room temperature afforded nearly quantitatively perhydro-1,3-benzoxazines **1–4**, which were transformed into the amides **5a–g** by acylation with acryloyl, methacryloyl, or crotonyl chloride and triethylamine or TMEDA in CH_2Cl_2 at 0 °C.

Perhydro-1,3-benzoxazines **5a–g** proved to be unstable in the presence of acids, and purification must be done on silica gel deactivated with triethylamine; otherwise, these compounds epimerize at C-2 and partially hydrolyze to 8-(*N*-acryloyl)aminomenthol derivatives. This fact makes impossible the study of the ene reaction of these compounds in the presence of Lewis acids.

Fortunately, thermally induced ene cyclization reaction of **5a–e** occurred with excellent chemical yields and a

SCHEME 1



SCHEME 2

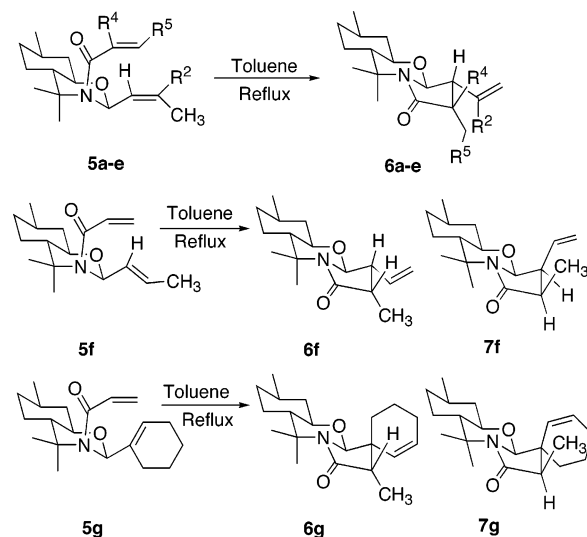


TABLE 1. Intramolecular Ene Reaction of Compounds **5a–g**

entry	amide	time (h)	yield ^a (%)	products (ratio) ^b
1	5a	5	95	6a (100)
2	5b	10	92	6b (100)
3	5c	30	86	6c (100)
4	5d	3	90	6d (100)
5	5e	15	90	6e (100)
6	5f	45	88	6f (72), 7f (28)
7	5g	60	85	6g (45), 7g (55)

^a Chemical yields refer to pure compounds after column chromatography. ^b Determined by integration of the signals in ¹H NMR spectra of the reaction mixtures.

high degree of stereocontrol (Scheme 2 and Table 1). Thus, perhydro-1,3-benzoxazines **5a–g** were transformed into the cyclization products **6a–g** and **7f–g** by refluxing in toluene with K_2CO_3 to prevent epimerization of starting materials.

The reactivity of perhydrobenzoxazines varied depending on the substitution pattern of the double bond at C-2. Perhydrobenzoxazines **5a–e**, with two substituents at the terminal position of this double bond, react with total diastereoselectivity leading to **6a–e** as single diastereomers in excellent yields (entries 1–5 in Table 1).

(12) For recent examples, see: (a) Matsubara, R.; Nakamura, Y.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3258. (b) Guo, H.; Wang, X.; Ding, K. *Tetrahedron Lett.* **2004**, *45*, 2009. (c) Aikawa, K.; Kainuma, S.; Hatano, M.; Mikami, K.; *Tetrahedron Lett.* **2004**, *45*, 183. (d) Caplan, N. A.; Hancock, F. E.; Bulman Page, P. C.; Hutchings, G. *J. Angew. Chem., Int. Ed.* **2004**, *43*, 1685. (e) Yuan, Y.; Zhang, X.; Ding, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 5478. (f) Ruck, R. T.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2003**, *42*, 4771. (g) Lei, A.; He, M.; Zhang, X. *J. Am. Chem. Soc.*, **2002**, *124*, 8198. (h) Kezuka, S.; Ikeno, T.; Yamada, T. *Org. Lett.* **2001**, *3*, 1937. (i) Koh, J. H.; Larsen, A. O.; Gagné, M. R. *Org. Lett.* **2001**, *3*, 1233. (j) Evans, D. A.; Tregay, S. W.; Burgey, C. S.; Paras, N. A.; Wojkovsky, T. J. *J. Am. Chem. Soc.* **2000**, *122*, 7936.

(13) (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876. (b) Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021. See also refs 1 and 10.

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(17) For other examples of preparation of 3,4-disubstituted pyrrolidines by intramolecular ene reaction, see: (a) Oppolzer, W.; Thirring, K. *J. Am. Chem. Soc.* **1982**, *104*, 4978. (b) Overman, L. E.; Lesuisse, D. *Tetrahedron Lett.* **1985**, *26*, 4167. (c) Lei, A.; Waldkirch, J. P.; He, M.; Zhang, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 4526. (d) Cao, P.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 6490. (e) Choony, N.; Sammes, P. G.; Smith, G.; Ward, R. W. *Chem. Commun.* **2001**, 6062. See too refs 10 and 14.

(18) Southon, I. W.; Buckingham, J., Eds. *Dictionary of Alkaloids*; Chapman and Hall: New York, 1989.

(19) For some examples of enantioselective synthesis of *trans*-3,4-disubstituted pyrrolidines, see: (a) Denmark, S. E.; Marcin, L. R. *J. Org. Chem.* **1995**, *60*, 3221. (b) Andrés, C.; Duque-Soladana, J. P.; Pedrosa, R. *Chem. Commun.* **1999**, 31. (c) Karlsson, S.; Han, F.; Höglberg, H.-E.; Caldirola, P. *Tetrahedron: Asymmetry* **1999**, *10*, 2605. (d) Karlsson, S.; Höglberg, H.-E. *Tetrahedron: Asymmetry* **2001**, *12*, 1975. (e) Karlsson, S.; Höglberg, H.-E. *Tetrahedron: Asymmetry* **2001**, *12*, 1977. (f) Johnson, T. A.; Jang, D. O.; Slafer, B. W.; Curtis, M. D.; Beak, P. *J. Am. Chem. Soc.* **2002**, *124*, 11689. (g) Galeazzi, R.; Martelli, G.; Mobbili, G.; Orena, M.; Rinaldi, S. *Tetrahedron: Asymmetry* **2003**, *14*, 3353.

In contrast, perhydrobenzoxazine **5f**, with only a methyl group at the double bond, reacts slower (entry 6) yielding a mixture (ca. 2.6:1) of two diastereomers **6f** and **7f**, whereas the cyclohexene derivative **5g** cyclizes to an almost equimolar mixture of diastereomeric spirocycles **6g** and **7g** (entry 7).

It is noteworthy that although the induced diastereoselectivity for ene cyclization of **5f** and **5g** was low, the simple diastereoselectivity was complete for the formation of the *cis*-2,3-disubstituted products. This result is in agreement with the general stereochemical trend for kinetically controlled thermal or Lewis acid mediated intramolecular ene reaction of 1,6-hexadienes to form *cis*-disubstituted adducts as major diastereomers.²⁰

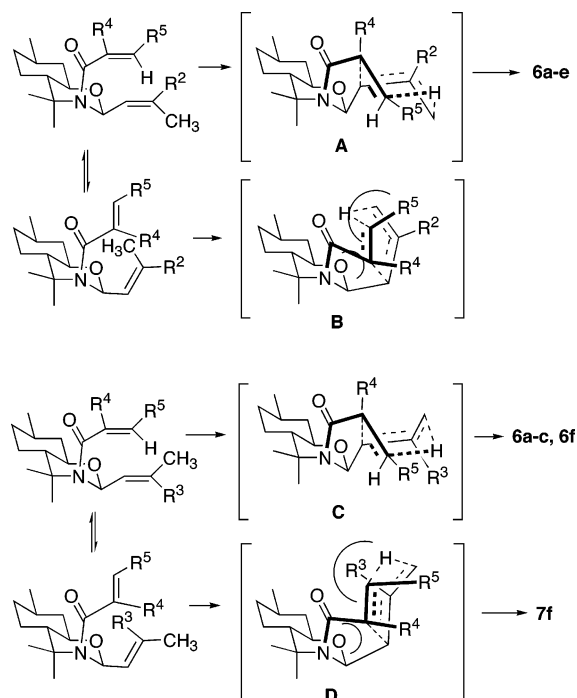
The influence of a methyl group at the enophile was tested in methacryloyl derivatives **5b** and **5e**, and in crotonyl derivative **5c**. As expected, they reacted slower than **5a** and **5d** and longer reaction times were necessary, probably due of steric hindrance and the electron-donating effect of the methyl group that make the enophile less reactive.²¹ However, the reaction was totally diastereoselective, and only a single isomer was obtained.

Interestingly, intramolecular ene reactions of compounds **5a–g** occur with total regioselectivity, providing the cyclic compounds that arise from a type I ene cyclization reaction,²² and type IV²³ or type II adducts for amide **5g** were not observed.

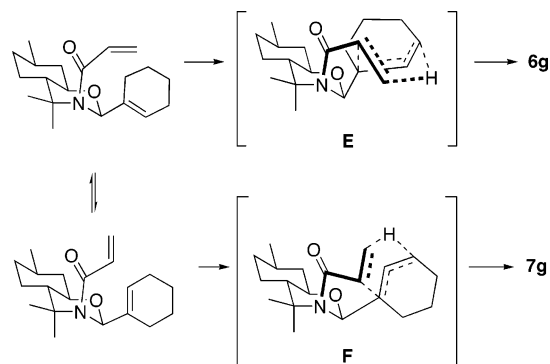
The stereochemistry of cycloadducts was assigned on the basis of COSY and NOESY experiments after isolation and purification by flash chromatography. The NOESY contacts allowed the assignment of the substituents at C-3, C-4, and the hydrogen atom at C-5 with a *cis* relationship for compounds **6a,c,d,f,g** in the pyrrolidin-2-one ring. In contrast, the double bond at C-4 and the substituent at C-3 are also *cis* for the spirocycle **7g**, but *trans* with respect to the hydrogen at C-5.²⁴

The formation of the *cis* stereoisomers can be explained by accepting that the reaction is a concerted process.²⁵ In this way, two *exo* (**A** and **B**) and two *endo* (**C** and **D**) transition states depending on the methyl group *cis* or *trans* that participate in the ene reaction can be envisaged. Whereas the observed ene adducts **6a–c** were obtained from transition states *exo-A* or *endo-C* that lead to the same product, transition states *exo-B* and *endo-D* are sterically less favorable due to the steric hindrance between the methyl group of the ene component in **B**, or the substituent R³ in **D**, and the benzoxazine framework, and no products were formed from these conformations

SCHEME 3



SCHEME 4



(Scheme 3). For amides **5d** and **5e** with a single *cis*-methyl group at the ene component only two different transition states (*exo-A* and *exo-B*) can be considered, and the stereoisomers formed (**6d** and **6e**) must arise from transition state *exo-A* due to the same reasons discussed above.

The same steric factors govern the formation of a mixture of diastereoisomers **6f** and **7f** from amide **5f**, with only one *trans*-methyl group at the ene component. In this case, it is possible to consider only two different *endo* transition states **C** and **D**. The major diastereomer **6f** will be formed from the most stable transition state **C**, but the steric constrain in *endo-D* (R³ = H) is smaller than for compounds **5a–e** and then **7f** is formed as minor diastereomer.

In the same way, the ene reaction of amide **5g** occurs through *endo* transition states **E** and **F** (Scheme 4); both of them are similar hindered and almost an equimolecular mixture of diastereomeric spirocycles **6g** and **7g** was obtained.

The transformation of the ene adducts **6a–g** into the final enantiopure 3,4-disubstituted pyrrolidines was achieved in two steps as depicted in Scheme 5. Treatment

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(21) Duncia, J. V.; Lansbury, P. T.; Miller, T., Jr.; Snider, B. B. *J. Am. Chem. Soc.* **1982**, 104, 1930.

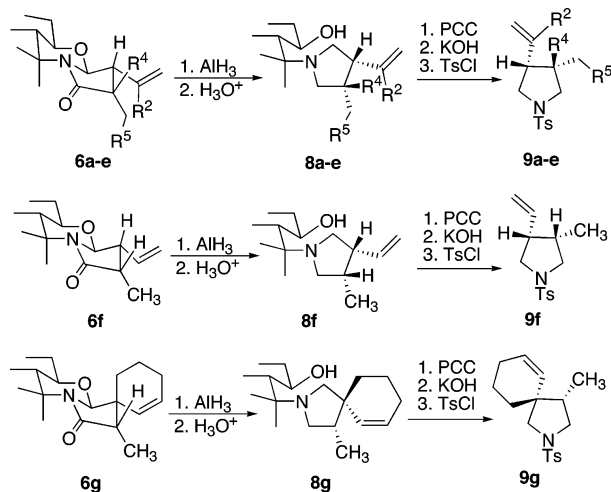
(22) Oppolzer classified intramolecular ene reactions into type I, II, and III depending on the positioning of the bridge linking the enophile and the ene component. Later, Snider observed additional type IV ene reaction. (a) Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, 17, 476. (b) Snider, B. B.; Duncia, J. V. *J. Org. Chem.* **1980**, 45, 3461.

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(24) See the Supporting Information.

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SCHEME 5



of the ene adducts with aluminum hydride in THF at -10°C furnished the aminomethanol derivatives **8a–g**, resulting from the ring opening *N,O*-acetal moiety and reduction of the amide group, in very good chemical yields (84–95%). These amino alcohols, upon oxidation with PCC in methylene chloride at room temperature, and treatment with 2.5 M solution of KOH in THF–MeOH–H₂O yielded the pyrrolidine derivatives. These compounds were isolated and characterized as the *N*-tosyl derivatives **9a–g** (48–62% from **8a–g**) by treatment with tosyl chloride and diisopropylethylamine.

In summary, the ene reaction on *N*-acryloyl-2-vinyl-substituted perhydro-1,3-benzoxazines constitutes a good diastereoselective entry for 3,4-disubstituted pyrrolidines easily transformed into enantiopure 3,4-disubstituted pyrrolidines. The enantiopure final products were obtained in 16–54% from the starting perhydro-1,3-benzoxazines.

Experimental Section

General Methods. All reactions were carried out under argon atmosphere in oven-dried glassware. Solvents were dried by standard methods: CH₂Cl₂ from CaH₂ and THF and toluene from Na. ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) were registered in CDCl₃ as solvent, and chemical shifts are given relative to TMS 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 F₂₅₄ indicator; the chromatograms were visualized under UV light and/or by staining with I₂ or phosphomolybdic acid. Flash chromatography was carried out on silica gel 60 (230–240 mesh).

Compounds **1**, **3**, **5a** and **5f**²⁶ and **2**, **5d** and **6a**¹⁵ have been previously described.

(2*S*,4*aS*,7*R*,8*aR*)-2-Cyclohexen-1-yl-4,4,7-trimethyloctahydrobenz[e][1,3]oxazine (4). Colorless oil. [α]_D²⁵ = +8.8 (c = 1.1, CH₂Cl₂). ¹H NMR (δ): 0.91 (d, 3H, J = 6.5 Hz); 0.95–1.19 (m, 4H); 1.09 (s, 3H); 1.10 (s, 3H); 1.46–1.70 (m, 8H); 1.91–2.28 (m, 5H); 3.45 (td, 1H, J_1 = 4.2 Hz, J_2 = 10.6 Hz); 4.62 (s, 1H); 5.82 (m, 1H). ¹³C NMR (δ): 19.4; 22.2; 22.3 (2C); 23.9; 24.7; 25.5; 29.8; 31.2; 34.9; 41.5; 51.1; 51.6; 74.8; 85.3; 123.8; 136.6. IR (film): 3320, 3090, 1650, 820, 790, 780,

760, 645 cm⁻¹. Anal. Calcd for C₁₇H₂₉NO: C, 77.51; H, 11.10; N, 5.32. Found: C, 77.80; H, 10.96; N, 5.47.

(2*S*,4*aS*,7*R*,8*aR*)-*N*-Methacryloyl-2-(2-methylpropenyl)-4,4,7-trimethyloctahydrobenz[e][1,3]oxazine (5b). Colorless oil. [α]_D²⁵ = +53.1 (c = 1.1, CH₂Cl₂). ¹H NMR (δ): 0.84–1.18 (m, 2H); 0.92 (d, 3H, J = 6.5 Hz); 1.35–1.60 (m, 2H); 1.48 (s, 3H); 1.62 (s, 3H); 1.65 (s, 3H); 1.69–1.87 (m, 2H); 1.73 (s, 3H); 1.89–2.02 (m, 2H); 1.90 (s, 3H); 3.62 (td, 1H, J_1 = 11.3 Hz, J_2 = 4.0 Hz); 4.98 (s, 1H); 5.05 (s, 1H); 5.40 (d, 1H, J = 5.6 Hz); 5.72 (d, 1H, J = 5.6 Hz). ¹³C NMR (δ): 18.3; 18.5; 20.0; 21.9; 25.1; 25.4; 25.6; 31.5; 34.6; 43.1; 47.2; 57.9; 73.4; 80.4; 114.9; 127.4; 136.3; 142.6; 172.2. IR (film): 2910, 1645, 1610, 1450, 1360, 940, 840, 810 cm⁻¹. Anal. Calcd for C₁₉H₃₁NO₂: C, 74.71; H, 10.23; N, 4.95. Found: C, 74.87; H, 10.38; N, 5.09.

(2*S*,4*aS*,7*R*,8*aR*)-*N*-Crotonyl-2-(2-methylpropenyl)-4,4,7-trimethyloctahydrobenz[e][1,3]oxazine (5c). Colorless oil. [α]_D²⁵ = +48.7 (c = 1.5, CH₂Cl₂). ¹H NMR (δ): 0.92 (d, 3H, J = 6.5 Hz); 0.95–1.46 (m, 3H); 1.48–1.84 (m, 2H); 1.49 (s, 3H); 1.60 (s, 3H); 1.74 (s, 3H); 1.77 (s, 3H); 1.81 (dd, 3H, J = 6.8 Hz, J_2 = 1.6 Hz); 1.87–1.98 (m, 3H); 3.60 (td, 1H, J_1 = 11.4 Hz, J_2 = 4 Hz); 5.45 (d, 1H, J = 5.6 Hz); 5.76 (d, 1H, J = 5.6 Hz); 5.94 (dq, 1H, J_1 = 15.0 Hz, J_2 = 1.6 Hz); 6.72 (dq, 1H, J_1 = 15.0 Hz, J_2 = 6.8 Hz). ¹³C NMR (δ): 18.1; 18.6; 19.0; 21.9; 24.7; 25.3; 25.6; 31.6; 34.6; 43.1; 46.9; 57.6; 73.1; 79.6; 125.3; 127.5; 137.5; 139.7; 166.3. IR (film): 2920, 1640, 1610, 1450, 1360, 960, 830 cm⁻¹. Anal. Calcd for C₁₉H₃₁NO₂: C, 74.71; H, 10.23; N, 4.95. Found: C, 74.62; H, 10.34; N, 4.82.

(2*S*,4*aS*,7*R*,8*aR*)-*N*-Methacryloyl-2-(*trans*-2-phenylpropen-1-yl)-4,4,7-trimethyloctahydrobenz[e][1,3]oxazine (5e). Colorless oil. [α]_D²⁵ = +25.5 (c = 4.6, CHCl₃). ¹H NMR (δ): 0.88–1.20 (m, 3H); 0.89 (d, 3H, J = 6.5 Hz); 1.38–1.52 (m, 1H); 1.53 (s, 3H); 1.68 (s, 3H); 1.74–1.82 (m, 2H); 1.93 (s, 3H); 1.97–2.05 (m, 2H); 2.09 (s, 3H); 3.69 (td, 1H, J_1 = 10.0 Hz, J_2 = 3.9 Hz); 5.05 (d, 1H, J = 1.4 Hz); 5.08 (d, 1H, J = 1.4 Hz); 5.91 (d, 1H, J = 5.4 Hz); 5.95 (d, 1H, J = 5.4 Hz); 7.26–7.37 (m, 5H). ¹³C NMR (δ): 16.5; 18.2; 20.0; 21.8; 25.1; 25.3; 31.5; 34.5; 42.9; 47.3; 57.9; 73.4; 80.4; 115.1; 125.6 (2C); 127.4; 128.3 (2 C); 129.8; 138.5; 142.4 (2C); 172.0. IR (film): 3080, 3050, 2925, 1645, 1630, 760, 735, 700 cm⁻¹. Anal. Calcd for C₂₄H₃₃NO₂: C, 78.43; H, 9.05; N, 3.81. Found: C, 78.29; H, 9.17; N, 3.98.

(2*S*,4*aS*,7*R*,8*aR*)-*N*-Acryloyl-2-cyclohexen-1-yl-4,4,7-trimethyloctahydrobenz[e][1,3]oxazine (5g). Colorless oil. [α]_D²⁵ = +52.9 (c = 1.7, CHCl₃). ¹H NMR (δ): 0.83–1.27 (m, 5H); 0.93 (d, 3H, J = 6.5 Hz); 1.43 (m, 1H); 1.53 (s, 3H); 1.58–1.77 (m, 5H); 1.63 (s, 3H); 1.92–2.11 (m, 4H); 2.18–2.30 (m, 1H); 3.66 (td, 1H, J_1 = 11.5 Hz, J_2 = 3.9 Hz); 5.39–5.40 (m, 1H); 5.55 (dd, 1H, J_1 = 7.7 Hz, J_2 = 4.8 Hz); 5.83–5.86 (m, 1H); 6.19 (d, 1H, J = 7.7 Hz); 6.20 (d, 1H, J = 4.8 Hz). ¹³C NMR (δ): 19.0; 22.0; 22.2; 23.7; 24.9; 25.1; 25.6; 31.6; 34.6; 43.1; 45.3; 57.7; 73.9; 85.3; 124.8; 126.8; 131.2; 139.5; 166.9. IR (film): 3050, 2980, 1670, 1630, 970, 820 cm⁻¹. Anal. Calcd for C₂₀H₃₁NO₂: C, 75.67; H, 9.84; N, 4.41. Found: C, 75.82; H, 9.71; N, 4.54.

Intramolecular Ene–Cyclization Reactions. General Procedure. A mixture of the amide (15 mmol), K₂CO₃ (1.0 g), and toluene (50 mL) was refluxed until the reaction was finished (TLC, 3–60 h). The solvent was eliminated under reduced pressure, and the residue was chromatographed on silica gel with hexane/EtOAc as eluent. Adduct **6d**¹⁵ has been previously described.

(2*S*,3*S*,3*aS*,4*aR*,6*R*,8*aS*)-3-Isopropenyl-2,6,9,9-tetramethyloctahydro-4*aH*-pyrrololo[2,1-*b*][1,3]benzoxazin-1(2*H*)-one (6a). Colorless solid. Mp: 92–93°C (from pentane). [α]_D²⁵ = –173.5 (c = 1.0, CH₂Cl₂). ¹H NMR (δ): 0.91–1.15 (m, 3H); 0.93 (d, 3H, J = 7.4 Hz); 0.94 (d, 3H, J = 6.5 Hz); 1.20 (s, 3H); 1.28 (m, 1H); 1.49 (m, 1H); 1.62–1.80 (m, 2H); 1.72 (s, 3H); 1.74 (s, 3H); 2.01 (m, 1H); 2.62 (qd, 1H, J_1 = 8.4 Hz, J_2 = 7.4 Hz); 2.69 (dd, 1H, J_1 = 8.4 Hz, J_2 = 6.3 Hz); 3.43 (td, 1H, J_1 = 10.6 Hz, J_2 = 4.2 Hz); 4.84 (s, 1H); 4.98 (d, 1H, J = 6.3 Hz). ¹³C NMR (δ): 11.8; 18.3; 21.9; 22.7; 23.9; 25.5; 31.1; 34.3; 38.9; 41.0; 48.5; 49.7; 56.7; 76.2; 85.6; 112.2; 140.1; 175.2. IR

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(Nujol dispersion): 3090, 1680, 790, 770, 750, 730 cm^{-1} . Anal. Calcd for $\text{C}_{18}\text{H}_{29}\text{NO}_2$: C, 74.18; H, 10.03; N, 4.81. Found: C, 74.31; H, 10.18; N, 4.94.

(3R,3aS,4aR,6R,8aS)-3-Isopropenyl-2,2,6,9,9-pentamethyloctahydro-4aH-pyrrolo[2,1-b][1,3]benzoxazin-1(2H)-one (6b). Colorless solid. Mp: 126–127°C (from pentane). $[\alpha]^{25}_{\text{D}} = -116.0$ ($c = 1.1$, CH_2Cl_2). ^1H NMR (δ): 0.80–1.11 (m, 3H); 0.82 (s, 3H); 0.90 (d, 3H, $J = 6.5$ Hz); 1.15 (s, 3H); 1.22 (s, 3H); 1.28 (m, 1H); 1.46 (m, 1H); 1.63–1.73 (m, 2H); 1.70 (s, 3H); 1.78 (s, 3H); 1.99 (m, 1H); 2.37 (d, 1H, $J = 7.8$ Hz); 3.37 (td, 1H, $J_1 = 10.7$ Hz, $J_2 = 4.1$ Hz); 4.80 (s, 1H); 4.87 (d, 1H, $J = 7.8$ Hz); 4.99 (s, 1H). ^{13}C NMR (δ): 17.9; 20.2; 21.9; 23.7; 23.9; 25.2; 25.6; 31.2; 34.4; 41.0; 43.5; 49.6; 55.5; 56.5; 77.4; 84.7; 113.5; 139.8; 177.1. IR (Nujol dispersion): 3085, 1700, 1640, 790, 770, 750, 720 cm^{-1} . Anal. Calcd for $\text{C}_{19}\text{H}_{31}\text{NO}_2$: C, 74.71; H, 10.23; N, 4.59. Found: C, 74.62; H, 10.35; N, 4.73.

(2S,3S,3aS,4aR,6R,8aS)-3-Isopropenyl-2-ethyl-6,9,9-trimethyloctahydro-4aH-pyrrolo[2,1-b][1,3]benzoxazin-1(2H)-one (6c). Colorless solid. Mp: 89–90°C (from pentane). $[\alpha]^{25}_{\text{D}} = -146.1$ ($c = 1.1$, CH_2Cl_2). ^1H NMR (δ): 0.85–1.13 (m, 3H); 0.93 (d, 3H, $J = 6.5$ Hz); 0.94 (t, 3H, $J = 7.4$ Hz); 1.22 (s, 3H); 1.28 (m, 1H); 1.45 (qd, 2H, $J_1 = 7.4$ Hz, $J_2 = 6.3$ Hz); 1.48–1.80 (m, 3H); 1.72 (s, 3H); 1.75 (s, 3H); 2.01 (m, 1H); 2.50 (dt, 1H, $J_1 = 8.7$ Hz, $J_2 = 6.3$ Hz); 2.76 (dd, 1H, $J_1 = 8.7$ Hz, $J_2 = 6.0$ Hz); 3.44 (td, 1H, $J_1 = 10.6$ Hz, $J_2 = 4.2$ Hz); 4.87 (s, 1H); 4.98 (d, 1H, $J = 6.0$ Hz); 4.99 (s, 1H). ^{13}C NMR (δ): 12.0; 18.9; 20.2; 21.9; 22.4; 24.0; 25.5; 31.1; 34.4; 41.0; 45.0; 48.5; 49.9; 57.0; 76.2; 86.2; 112.8; 140.2; 174.6. IR (Nujol dispersion): 3090, 1720, 705 cm^{-1} . Anal. Calcd for $\text{C}_{19}\text{H}_{31}\text{NO}_2$: C, 74.71; H, 10.23; N, 4.59. Found: C, 74.84; H, 10.38; N, 4.71.

(3R,3aS,4aR,6R,8aS)-3-(1-Phenylvinyl)-2,2,6,9,9-pentamethyloctahydro-4aH-pyrrolo[2,1-b][1,3]benzoxazin-1(2H)-one (6e). Colorless solid. Mp: 163–164°C (from hexane). $[\alpha]^{25}_{\text{D}} = -16.4$ ($c = 1.2$, CH_2Cl_2). ^1H NMR (δ): 0.82 (s, 3H); 0.83 (s, 3H); 0.92–1.16 (m, 3H); 0.95 (d, 3H, $J = 6.5$ Hz); 1.21 (s, 3H); 1.35 (m, 1H); 1.50 (m, 1H); 1.74–1.77 (m, 2H); 1.76 (s, 3H); 2.06 (m, 1H); 3.08 (d, 1H, $J = 7.7$ Hz); 3.45 (td, 1H, $J_1 = 10.6$ Hz, $J_2 = 4.1$ Hz); 5.04 (d, 1H, $J = 7.7$ Hz); 5.17 (s, 1H); 5.34 (s, 1H); 7.26–7.36 (m, 5H). ^{13}C NMR (δ): 17.8; 20.5; 21.9; 23.8; 24.9; 25.6; 31.1; 34.3; 41.0; 43.5; 49.5; 53.3; 56.4; 77.4; 85.0; 114.6; 127.0 (2C); 127.4; 128.0 (2C); 142.6; 144.7; 176.8. IR (Nujol dispersion): 3090, 1685, 1610, 780, 710 cm^{-1} . Anal. Calcd for $\text{C}_{24}\text{H}_{33}\text{NO}_2$: C, 78.43; H, 9.05; N, 3.81. Found: C, 78.28; H, 9.22; N, 3.65.

(2S,3R,3aS,4aR,6R,8aS)-2,6,9,9-Tetramethyl-3-vinyloctahydro-4aH-pyrrolo[2,1-b][1,3]benzoxazin-1(2H)-one (6f). Colorless oil. $[\alpha]^{25}_{\text{D}} = -97.9$ ($c = 1.1$, CH_2Cl_2). ^1H NMR (δ): 0.86–1.13 (m, 3H); 0.93 (d, 3H, $J = 6.5$ Hz); 1.02 (d, 3H, $J = 7.6$ Hz); 1.18 (s, 3H); 1.28 (m, 1H); 1.49 (m, 1H); 1.60–1.79 (m, 2H); 1.73 (s, 3H); 2.01 (m, 1H); 2.60 (dq, 1H, $J_1 = 8.7$ Hz, $J_2 = 7.6$ Hz); 2.75 (td, 1H, $J_1 = 8.7$ Hz, $J_2 = 6.3$ Hz); 3.40 (td, 1H, $J_1 = 10.6$ Hz, $J_2 = 4.2$ Hz); 4.78 (d, 1H, $J = 6.3$ Hz); 5.22 (d, 1H, $J = 10.3$ Hz); 5.23 (d, 1H, $J = 17.2$ Hz); 5.74 (ddd, 1H, $J_1 = 8.7$ Hz, $J_2 = 10.3$ Hz, $J_3 = 17.2$ Hz). ^{13}C NMR (δ): 12.3; 18.5; 21.9; 23.9; 25.4; 31.1; 34.3; 40.1; 40.9; 46.2; 49.7; 56.8; 76.2; 87.5; 118.7; 133.7; 175.6. IR (film): 3090, 2940, 1710, 760, 720 cm^{-1} . Anal. Calcd for $\text{C}_{17}\text{H}_{27}\text{NO}_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.76; H, 9.92; N, 5.18.

(2'S,3'R,3a'S,4a'R,6'R,8a'S)-2',6',9',9'-Tetramethyloctahydro-4a'H-spiro[cyclohex-2-ene-1,3'-pyrrolo[2,1-b]-[1,3]benzoxazin]-1'(2'H)-one (6g). Colorless solid. Mp: 153–154 °C (from pentane). $[\alpha]^{25}_{\text{D}} = -43.9$ ($c = 1.0$, CHCl_3). ^1H NMR (δ): 0.88–1.13 (m, 3H); 0.93 (d, 3H, $J = 6.5$ Hz); 1.01 (d, 3H, $J = 7.6$ Hz); 1.18 (s, 3H); 1.25–1.73 (m, 7H); 1.72 (s, 3H); 1.91–2.03 (m, 4H); 2.30 (q, 1H, $J = 7.6$ Hz); 3.40 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.2$ Hz); 4.68 (s, 1H); 5.40 (d, 1H, $J = 10.2$ Hz); 5.88 (dt, 1H, $J_1 = 10.2$ Hz, $J_2 = 3.6$ Hz). ^{13}C NMR (δ): 11.3; 19.0; 19.3; 22.0; 24.1; 25.0; 25.6; 27.4; 31.2; 34.4; 41.0; 42.2; 47.3; 50.1; 57.0; 76.1; 89.9; 128.6; 130.7; 176.4. IR (Nujol dispersion): 3060, 1700, 700 cm^{-1} . Anal. Calcd. for $\text{C}_{20}\text{H}_{31}\text{NO}_2$: C, 75.67; H, 9.84; N, 4.41. Found: C, 75.83; H, 9.96; N, 4.54.

(2R,3S,3aS,4aR,6R,8aS)-2,6,9,9-Tetramethyl-3-vinyloctahydro-4aH-pyrrolo[2,1-b][1,3]benzoxazin-1(2H)-one (7f). Purity 90%. Colorless oil. ^1H NMR (δ): 0.83–1.12 (m, 3H); 0.93 (d, 3H, $J = 6.5$ Hz); 1.03 (d, 3H, $J = 7.4$ Hz); 1.18 (s, 3H); 1.27 (m, 1H); 1.49 (m, 1H); 1.68–1.80 (m, 2H); 1.72 (s, 3H); 1.98 (m, 1H); 2.41 (dq, $J_1 = 7.9$ Hz, $J_2 = 7.4$ Hz); 3.00 (ddd, 1H, $J_1 = 10.2$ Hz, $J_2 = 7.9$ Hz, $J_3 = 5.5$ Hz); 3.39 (td, 1H, $J_1 = 10.5$ Hz, $J_2 = 4.3$ Hz); 4.93 (d, 1H, $J = 5.5$ Hz); 5.12 (dd, 1H, $J_1 = 17.0$ Hz, $J_2 = 1.7$ Hz); 5.17 (dd, 1H, $J_1 = 10.2$ Hz, $J_2 = 1.7$ Hz); 5.71 (dt, 1H, $J_1 = 17.0$ Hz, $J_2 = 10.2$ Hz). ^{13}C NMR (δ): 11.5; 18.1; 22.0; 23.9; 25.7; 31.2; 34.4; 40.2; 40.9; 46.2; 49.7; 56.7; 76.0; 85.5; 118.5; 132.7; 175.5. IR (film): 3075, 2930, 1700, 1460, 760.

(2'R,3'S,3a'S,4a'R,6'R,8a'S)-2',6',9',9'-Tetramethyloctahydro-4a'H-spiro[cyclohex-2-ene-1,3'-pyrrolo[2,1-b][1,3]benzoxazin]-1'(2'H)-one (7g). Colorless solid. Mp: 172–173 °C (from pentane). $[\alpha]^{25}_{\text{D}} = -99.0$ ($c = 0.8$, CHCl_3). ^1H NMR (δ): 0.86–1.14 (m, 3H); 0.93 (d, 3H, $J = 6.6$ Hz); 1.06 (d, 3H, $J = 7.3$ Hz); 1.16 (s, 3H); 1.23 (m, 1H); 1.44 (m, 1H); 1.59–1.80 (m, 6H); 1.70 (s, 3H); 1.90–2.07 (m, 4H); 3.35 (td, 1H, $J_1 = 10.6$ Hz, $J_2 = 4.3$ Hz); 4.52 (s, 1H); 5.44 (d, 1H, $J = 10.3$ Hz); 5.92 (dt, 1H, $J_1 = 10.3$ Hz, $J_2 = 3.6$ Hz). ^{13}C NMR (δ): 10.8; 17.8; 19.6; 21.9; 23.9; 24.8; 25.8; 31.2; 33.0; 34.3; 40.9; 43.8; 47.5; 49.3; 56.5; 75.8; 91.7; 125.3; 130.1; 175.0. IR (Nujol dispersion): 3070, 1700, 690 cm^{-1} . Anal. Calcd for $\text{C}_{20}\text{H}_{31}\text{NO}_2$: C, 75.67; H, 9.84; N, 4.41. Found: C, 75.83; H, 10.01; N, 4.32.

(3S,4S)-N-(8-Mentholyl)-3-isoprenyl-4-methylpyrrolidine (8a). Yield: 87%. Colorless solid. Mp: 64–65°C (from AcOEt/hexane). $[\alpha]^{25}_{\text{D}} = -57.8$ ($c = 1.1$, CH_2Cl_2). ^1H NMR (333 K) (δ): 0.78 (d, 3H, $J = 6.9$ Hz); 0.82–1.07 (m, 3H); 0.91 (d, 3H, $J = 6.5$ Hz); 0.95 (s, 3H); 1.17 (s, 3H); 1.39–1.52 (m, 2H); 1.55–1.69 (m, 2H); 1.71 (s, 3H); 1.93 (m, 1H); 2.32 (m, 1H); 2.47 (m, 1H); 2.61 (m, 1H); 2.85–2.92 (m, 2H); 3.13 (m, 1H); 3.62 (td, 1H, $J_1 = 10.1$ Hz, $J_2 = 3.9$ Hz); 4.66 (s, 1H); 4.84 (s, 1H); 8.51 (s broad, 1H). ^{13}C NMR (333 K) (δ): 14.5; 16.5; 21.3; 21.9; 22.8; 25.5; 30.9; 33.4; 35.1; 44.3; 46.1; 47.9; 48.8; 53.1; 59.0; 72.6; 110.6; 143.2. IR (Nujol dispersion): 3300 (broad), 1630 cm^{-1} . Anal. Calcd for $\text{C}_{18}\text{H}_{33}\text{NO}$: C, 77.36; H, 11.90; N, 5.01. Found: C, 77.48; H, 12.03; N, 4.90.

(4R)-N-(8-Mentholyl)-4-isoprenyl-3,3-dimethylpyrrolidine (8b). Yield: 88%. Colorless oil. $[\alpha]^{25}_{\text{D}} = -21.1$ ($c = 0.8$, CH_2Cl_2). ^1H NMR (333 K) (δ): 0.87–1.11 (m, 3H); 0.88 (s, 3H); 0.90 (d, 3H, $J = 6.5$ Hz); 0.95 (s, 3H); 1.10 (s, 3H); 1.16 (s, 3H); 1.32–1.49 (m, 2H); 1.55–1.69 (m, 2H); 1.75 (s, 3H); 1.92 (m, 1H); 2.30 (dd, 1H, $J_1 = 9.3$ Hz, $J_2 = 8.8$ Hz); 2.54 (d, 1H, $J = 8.8$ Hz); 2.69 (m, 1H); 2.91–3.02 (m, 2H); 3.63 (td, 1H, $J_1 = 10.2$ Hz, $J_2 = 4.0$ Hz); 4.72 (s, 1H); 4.88 (s, 1H); 8.50 (s broad, 1H). ^{13}C NMR (333 K) (δ): 16.5; 21.2; 21.9 (2C); 22.8; 23.6; 25.6; 30.9; 35.1; 39.6; 44.4; 48.6; 48.7; 54.3; 59.2; 60.7; 72.7; 112.2; 142.8. IR (film): 3300 (broad), 1625 cm^{-1} . Anal. Calcd for $\text{C}_{19}\text{H}_{35}\text{NO}$: C, 77.76; H, 12.02; N, 4.77. Found: C, 77.60; H, 12.16; N, 4.59.

(3S,4S)-N-(8-Mentholyl)-3-ethyl-4-isopropenylpyrrolidine (8c). Yield: 90%. Colorless oil. $[\alpha]^{25}_{\text{D}} = -44.6$ ($c = 1.0$, CH_2Cl_2). ^1H NMR (C_6D_6 , 351 K) (δ): 0.80 (s, 3H); 0.82–1.12 (m, 3H); 0.82 (t, 3H, $J = 7.3$ Hz); 0.92 (d, 3H, $J = 6.4$ Hz); 1.16 (s, 3H); 1.16–1.64 (m, 6H); 1.62 (s, 3H); 1.91 (m, 1H); 2.19 (m, 1H); 2.55–2.66 (m, 2H); 2.82–2.94 (m, 2H); 3.11 (m, 1H); 3.79 (td, 1H, $J_1 = 10.0$ Hz, $J_2 = 4.0$ Hz); 4.68 (s, 1H); 4.84 (s, 1H); 6.98 (s broad, 1H). ^{13}C NMR (C_6D_6 , 351 K) (δ): 12.3; 16.6; 21.1; 21.5; 21.8; 22.6; 25.8; 31.0; 35.2; 41.4; 44.8; 47.5; 47.8; 49.1; 50.3; 59.7; 72.3; 111.1; 143.3. IR (film): 3280 (broad), 1640 cm^{-1} . Anal. Calcd for $\text{C}_{19}\text{H}_{35}\text{NO}$: C, 77.76; H, 12.02; N, 4.77. Found: C, 77.89; H, 11.91; N, 4.89.

(4R)-N-(8-Mentholyl)-3,3-dimethyl-4-(1-phenylvinyl)pyrrolidine (8e). Yield: 96%. Colorless oil. $[\alpha]^{25}_{\text{D}} = +44.6$ ($c = 0.9$, CH_2Cl_2). ^1H NMR (333 K) (δ): 0.22 (s, 3H); 0.83–1.16 (m, 3H); 0.84 (s, 3H); 0.91 (d, 3H, $J = 6.5$ Hz); 0.98 (s, 3H); 1.18 (s, 3H); 1.40–1.49 (m, 2H); 1.50 (m, 1H); 1.68 (m, 1H); 1.96 (m, 1H); 2.55 (d, 1H, $J = 9.0$ Hz); 2.76 (m, 1H); 2.91–3.14 (m, 3H); 3.64 (td, 1H, $J_1 = 10.4$ Hz, $J_2 = 4.0$ Hz); 5.09 (s,

1H); 5.23 (s, 1H); 7.20–7.35 (m, 5H); 9.50 (s broad, 1H). ¹³C NMR (333 K) (δ): 16.5; 21.3; 21.9; 23.1; 25.6; 27.9; 30.9; 35.1; 39.5; 44.4; 48.6; 49.5; 51.6; 59.1; 61.1; 72.8; 113.9; 126.8 (2C); 127.0; 127.9 (2C); 144.0; 147.5. IR (film): 3385 (broad), 3085, 2950, 1625, 780, 700 cm⁻¹. Anal. Calcd for C₂₄H₃₇NO: C, 81.07; H, 10.49; N, 3.94. Found: C, 81.18; H, 10.36; N, 4.17.

(3R,4S)-N-(8-Mentholyl)-3-methyl-4-vinylpyrrolidine (8f). Yield: 84%. Colorless solid. Mp: 59–60 °C (from AcOEt/hexane). [α]_D²⁵ = -26.7 (c = 1.0, CH₂Cl₂). ¹H NMR (333 K) (δ): 0.82–1.11 (m, 3H); 0.88 (d, 3H, *J* = 6.8 Hz); 0.91 (d, 3H, *J* = 6.5 Hz); 0.94 (s, 3H); 1.16 (s, 3H); 1.31–1.52 (m, 2H); 1.53–1.74 (m, 2H); 1.92 (m, 1H); 2.21 (m, 1H); 2.33 (m, 1H); 2.60–2.78 (m, 2H); 2.98 (m, 1H); 3.08 (m, 1H); 3.62 (td, 1H, *J*₁ = 10.3 Hz, *J*₂ = 4.0 Hz); 3.67 (s, 1H); 5.00 (d, 1H, *J* = 16.1 Hz); 5.02 (d, 1H, *J* = 9.8 Hz); 5.74 (ddd, 1H, *J*₁ = 8.6 Hz, *J*₂ = 9.8 Hz, *J*₃ = 16.1 Hz). ¹³C NMR (333 K) (δ): 14.6; 16.7; 21.3; 21.8; 25.6; 30.9; 35.0; 35.1; 44.2; 45.2; 48.7; 52.8; 59.0; 63.5; 72.7; 115.4; 137.6. IR (Nujol dispersion): 3250 (broad), 1610. cm⁻¹. Anal. Calcd for C₁₇H₃₁NO: C, 76.92; H, 11.77; N, 5.28. Found: C, 77.07; H, 11.66; N, 5.37.

(4S,5R)-N-(8-Mentholyl)-4-methyl-2-azaspiro[4,5]dec-6-ene (8g). Yield: 85%. Colorless oil. [α]_D²⁵ = -30.0 (c = 1.2, CHCl₃). ¹H NMR (333 K) (δ): 0.85–1.09 (m, 3H); 0.88 (d, 3H, *J* = 7.5 Hz); 0.90 (d, 3H, *J* = 6.5 Hz); 0.91 (s, 3H); 1.13 (s, 3H); 1.32–1.69 (m, 8H); 1.84 (m, 1H); 1.89–1.98 (m, 3H); 2.27 (m, 1H); 2.59–2.66 (m, 2H); 3.16 (m, 1H); 3.62 (td, 1H, *J*₁ = 10.3 Hz, *J*₂ = 4.1 Hz); 5.47 (d, 1H, *J* = 10.2 Hz); 5.72 (dt, 1H, *J*₁ = 10.2 Hz, *J*₂ = 3.7 Hz); 8.45 (s broad, 1H). ¹³C NMR (333 K) (δ): 14.7; 16.9; 20.3; 21.3; 21.9; 25.1; 25.7; 31.0; 35.1; 36.0; 42.2; 42.9; 44.4; 48.4; 52.6; 58.6 (2C); 72.7; 127.3; 131.1. IR (film): 3300; 2980, 1610, 1450, 1380, 710. cm⁻¹. Anal. Calcd for C₂₀H₃₅NO: C, 78.63; H, 11.55; N, 4.58. Found: C, 78.51; H, 11.67; N, 4.61.

(3S,4S)-N-Tosyl-3-isoprenyl-4-methylpyrrolidine (9a). Yield: 58%. Colorless solid. Mp: 55–56 °C (from pentane). [α]_D²⁵ = +10.8 (c = 0.8, CH₂Cl₂). ¹H NMR (δ): 0.60 (d, 3H, *J* = 7.0 Hz); 1.64 (s, 3H); 2.32 (m, 1H); 2.45 (s, 3H); 2.57 (m, 1H); 3.13 (dd, 1H, *J*₁ = 9.6 Hz, *J*₂ = 2.6 Hz); 3.28 (t, 1H, *J* = 9.6 Hz); 3.38–3.48 (m, 2H); 4.55 (s, 1H); 4.83 (s, 1H); 7.30 (d, 2H, *J* = 8.3 Hz); 7.70 (d, 2H, *J* = 8.3 Hz). ¹³C NMR (δ): 13.2; 21.5; 22.7; 34.5; 48.2; 48.4; 54.8; 111.6; 127.3 (2C); 129.6 (2C); 134.1; 141.8; 143.2. IR (Nujol dispersion): 3100, 1590, 1170, 890, 810 cm⁻¹. Anal. Calcd for C₁₅H₂₁NO₂S: C, 64.48; H, 7.58; N, 5.01. Found: C, 64.59; H, 7.51; N, 4.90.

(4R)-N-Tosyl-4-isoprenyl-3,3-dimethylpyrrolidine (9b). Yield: 56%. Colorless oil. [α]_D²⁵ = +5.0 (c = 1.5, CH₂Cl₂). ¹H NMR (δ): 0.73 (s, 3H); 0.96 (s, 3H); 1.66 (s, 3H); 2.28 (t, 1H, *J* = 8.3 Hz); 2.43 (s, 3H); 3.01 (d, 1H, *J* = 9.6 Hz); 3.17 (d, 1H, *J* = 9.6 Hz); 3.35 (dd, 1H, *J*₁ = 8.3 Hz, *J*₂ = 9.9 Hz); 3.47 (dd, 1H, *J*₁ = 8.3 Hz, *J*₂ = 9.9 Hz); 4.60 (s, 1H); 4.85 (s, 1H); 7.33 (d, 2H, *J* = 8.2 Hz); 7.72 (d, 2H, *J* = 8.2 Hz). ¹³C NMR (δ): 21.4; 21.5; 23.3; 26.5; 41.2; 50.5; 54.0; 60.7; 113.5; 127.3 (2C); 129.6 (2C); 134.0; 141.7; 143.3. IR (film): 3080, 2920, 1600, 1500, 1160, 860, 800 cm⁻¹. Anal. Calcd for C₁₆H₂₃NO₂S: C, 65.49; H, 7.90; N, 4.77. Found: C, 65.63; H, 8.03; N, 4.82.

(3S,4S)-N-Tosyl-3-ethyl-4-isopropenylpyrrolidine (9c). Yield: 52%. Colorless oil. [α]_D²⁵ = +11.5 (c = 0.8, CH₂Cl₂). ¹H NMR (δ): 0.72 (m, 1H); 0.78 (t, 3H, *J* = 6.8 Hz); 1.14 (m, 1H); 1.63 (s, 3H); 1.99 (m, 1H); 2.43 (s, 3H); 2.63 (m, 1H); 3.22–3.44 (m, 4H); 4.54 (s, 1H); 4.81 (s, 1H); 7.32 (d, 2H, *J* = 8.2

Hz); 7.73 (d, 2H, *J* = 8.2 Hz). ¹³C NMR (δ): 12.4; 20.0; 21.5; 22.6; 42.5; 48.2; 49.4; 51.6; 112.1; 127.3 (2C); 129.5 (2C); 134.1; 142.2; 143.2. IR (film): 3060; 2920, 1600, 1500, 1170, 880, 810 cm⁻¹. Anal. Calcd for C₁₆H₂₃NO₂S: C, 65.49; H, 7.90; N, 4.77. Found: C, 65.52; H, 7.79; N, 4.65.

(4R)-N-Tosyl-3,3-dimethyl-4-(1-phenylvinyl)pyrrolidine (9e). Yield: 62%. Colorless oil. [α]_D²⁵ = +73.4 (c = 2.0, CH₂Cl₂). ¹H NMR (δ): 0.58 (s, 3H); 0.63 (s, 3H); 2.44 (s, 3H); 2.97 (t, 1H, *J* = 8.3 Hz); 3.06 (d, 1H, *J* = 9.7 Hz); 3.19 (d, 1H, *J* = 9.7 Hz); 3.49 (dd, 1H, *J*₁ = 8.3 Hz, *J*₂ = 9.9 Hz); 3.67 (dd, 1H, *J*₁ = 8.3 Hz, *J*₂ = 9.9 Hz); 4.93 (s, 1H); 5.23 (s, 1H); 7.19–7.30 (m, 5H); 7.35 (d, 2H, *J* = 8.2 Hz); 7.76 (d, 2H, *J* = 8.2 Hz). ¹³C NMR (δ): 21.3; 21.4; 26.3; 41.2; 51.0; 51.1; 60.9; 114.6; 126.5 (2C); 127.2 (2C); 127.4; 128.1; 129.5 (2C); 134.0; 143.0; 143.3; 146.1. IR (film): 3060, 3020, 2960, 1625, 1597, 1340, 1160, 1095, 780, 735, 705, 665 cm⁻¹. Anal. Calcd for C₂₁H₂₅NO₂S: C, 70.95; H, 7.09; N, 3.94. Found: C, 71.08; H, 6.98; N, 4.05.

(3R,4S)-N-Tosyl-3-methyl-4-vinylpyrrolidine (9f).²⁷ Yield: 50%. Colorless solid. Mp: 65–67 °C (from pentane). [α]_D²⁵ = +9.3 (c = 1.0, CH₂Cl₂). ¹H NMR (δ): 0.76 (d, 3H, *J* = 7.0 Hz); 2.20 (m, 1H); 2.44 (s, 3H); 2.65 (m, 1H); 2.97 (dd, 1H, *J*₁ = 6.1 Hz, *J*₂ = 9.8 Hz); 3.20 (dd, 1H, *J*₁ = 6.1 Hz, *J*₂ = 9.8 Hz); 3.38–3.44 (m, 2H); 4.98 (dd, 1H, *J*₁ = 17.0 Hz, *J*₂ = 1.0 Hz); 5.02 (dd, 1H, *J*₁ = 10.4 Hz, *J*₂ = 1.0 Hz); 5.49 (ddd, 1H, *J*₁ = 17.0 Hz, *J*₂ = 10.4 Hz, *J*₃ = 8.3 Hz); 7.33 (d, 2H, *J* = 8.1 Hz); 7.72 (d, 2H, *J* = 8.1 Hz). ¹³C NMR (δ): 13.5; 21.5; 36.5; 46.1; 51.3; 53.9; 117.0; 127.3 (2C); 129.6 (2C); 133.9; 135.0; 143.3. IR (Nujol dispersion): 3040, 1600, 1490, 1160, 1000, 910, 830 cm⁻¹. Anal. Calcd for C₁₄H₁₉NO₂S: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.23; H, 7.35; N, 5.26.

(4S,5R)-N-Tosyl-4-methyl-2-azaspiro[4,5]dec-6-ene (9g). Yield: 48%. Colorless oil. [α]_D²⁵ = +39.4 (c = 0.9, CHCl₃). ¹H NMR (δ): 0.78 (d, 3H, *J* = 7.2 Hz); 1.28–1.66 (m, 4H); 1.83 (m, 1H); 1.92–1.98 (m, 2H); 2.44 (s, 3H); 2.95 (dd, 1H, *J*₁ = 9.9 Hz, *J*₂ = 7.9 Hz); 3.05 (d, 1H, *J* = 9.7 Hz); 3.29 (d, 1H, *J* = 9.7 Hz); 3.50 (dd, 1H, *J*₁ = 9.9 Hz, *J*₂ = 7.9 Hz); 5.17 (d, 1H, *J* = 10.2 Hz); 5.68 (dt, 1H, *J*₁ = 3.7 Hz, *J*₂ = 10.2 Hz); 7.31 (d, 2H, *J* = 8.3 Hz); 7.71 (d, 2H, *J* = 8.3 Hz). ¹³C NMR (δ): 13.1; 20.2; 21.5; 25.0; 32.6; 42.3; 44.7; 53.5; 59.9; 127.4 (2C); 127.8; 129.1; 129.5 (2C); 133.8; 143.2. IR (film): 3060; 2980, 1610, 1460, 1350, 1180, 680 cm⁻¹. Anal. Calcd for C₁₇H₂₃NO₂S: C, 66.85; H, 7.59; N, 4.59. Found: C, 66.79; H, 7.68; N, 4.31.

Acknowledgment. We thank the Spanish Ministerio de Educación y Ciencia (DGICYT, Projects BQU2002-01046) for financial support. C.D.R. also thanks the MEC for a predoctoral fellowship (FPU).

Supporting Information Available: General experimental methods and copies of ¹H NMR for compounds **6a–g**, **7g**, and **9a–g** and COSY and NOESY experiments for compounds **6a–g** and **7g**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO050360A

(27) We thank one of the reviewer by the notice that this compound has been recently described as a mixture of stereoisomers: Hirashita, T.; Tanaka, J.; Hasashi, A.; Araki, S. *Tetrahedron Lett.* **2005**, *46*, 289.