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

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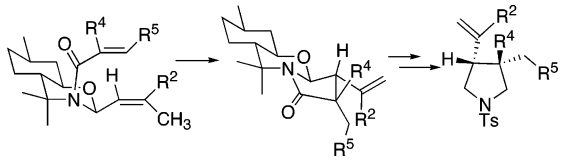

Chiral 3-acryloyl-2-vinyl-substituted 1,3-perhydrobenzoxazines derived from (−)-8-aminomenthol participate in an ene reaction leading to 3,4-disubstituted pyrrolidinone derivates with excellent diastereoselectivity. The cycloadducts were transformed into enantiopure 3,4-disubstituted pyrrolidines after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

Introduction

The ene reaction[1] 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 alkenes[2] (olefin−ene or Alder−ene reaction), carbonyl functionalities[3] (carbonyl−ene reaction), azo compounds,[4] singlet oxygen,[5] nitroso groups,[6] or phosphorus derivatives[7] as enophiles have been used in carbon−carbon and carbon−heteroatom transformations with olefins. Reactions involving hetero−ene components such as enoles[8] and enamines[9] 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 reaction[10] 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 centers[11] 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-benzoxacine derivative **5d** was easily transformed by

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(1) Carruthers, W. In *Cycloaddition Reactions in Organic Synthesis*; Pergamon Press: Oxford, 1990; p 241.

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(3) Snider, B. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon Press: Oxford, 1991; Vol. 2, p 527.

(4) For a rewiew 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.

(6) Adam, W.; Krebs, O. *Chem. Rev*. **2003**, *103*, 4131.

(7) For a review on phospha−ene reactions, see: Mackewitz, T. W.; Regitz, M. *Synthesis* **1998**, 125.

(8) For a review on Conia reaction, see: Conia, J. M.; Le Perchec, P. *Synthesis* **1975**, 1.

(9) Cossy, J.; Bouzide, A.; Pfau, M. *J. Org. Chem.* **1997**, *62*, 7106.

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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.; Rodriguez-Ranera, C.; Rodriguez-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.; Tereda, M.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949.

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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-aminomenthol[16] 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

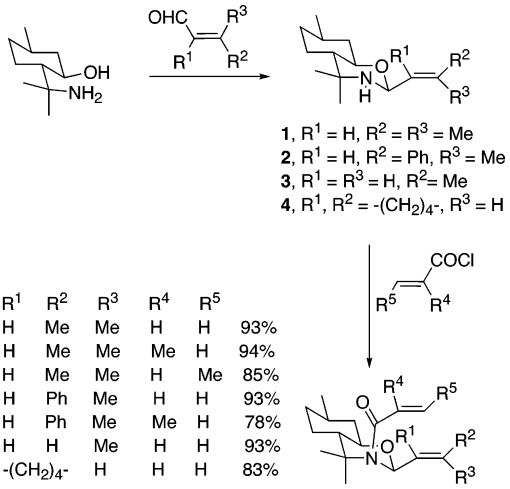
The starting chiral perhydro-1,3-benzoxazines **5a**−**g** were prepared in two steps as single diastereomers and in good chemical yields, as summarized in Scheme 1. Condensation of (−)-8-aminomenthol with α,β-unsaturated aldehydes in CH_2Cl_2 at room temperature afforded nearly quantitatively perhydro-1,3-benzoxazines **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 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).

SCHEME 1



SCHEME 2

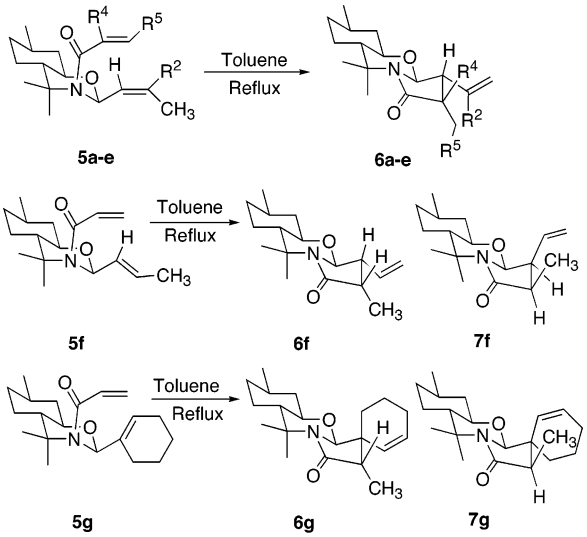


TABLE 1. Intramolecular Ene Reaction of Compounds 5a−g

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.

(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.

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(14) Pedrosa, R.; Andrés, C.; Rosón, C. D.; Vicente, M. *J. Org. Chem.* **2003**, *68*, 1852.

(15) Pedrosa, R.; Andrés, C.; Nieto, J. *J. Org. Chem.* **2002**, *67*, 782.

(16) Rassat, A.; Rey, P. *Tetrahedron* **1974**, *30*, 3315.

(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.; Högberg, H.-E.; Caldirola, P. *Tetrahedron: Asymmetry* **1999**, *10*, 2605. (d) Karlsson, S.; Högberg, H.-E. *Tetrahedron: Asymmetry* **2001**, *12*, 1975. (e) Karlsson, S.; Högberg, 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]

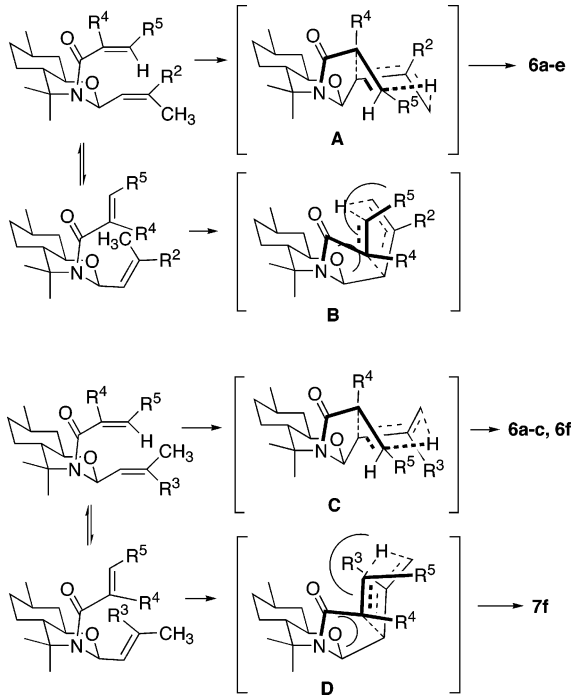
The influence of a methyl group at the enophile was tested in methacryloyl derivatives **5b** and **5e**, and in crotonyl derivative **5c**. As expected, they reacted slower than **5a** and **5d** and longer reaction times were necessary, probably due of steric hindrance and the electron-donating effect 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 IV[23] or type II adducts for amide **5g** were not observed.

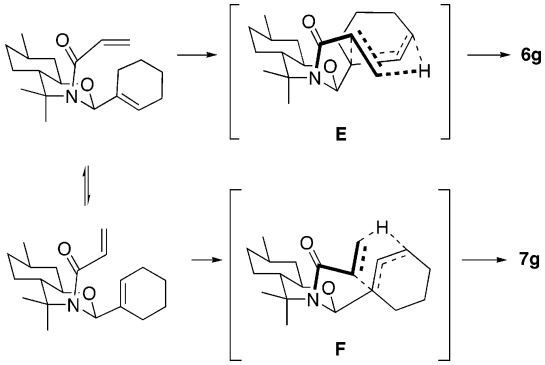
The stereochemistry of cycloadducts was assigned on the basis of COSY and NOESY experiments after isolation and purification by flash chromatography. The NOESY contacts allowed the assignation of the substituents at C-3, C-4, and the hydrogen atom at C-5 with a *cis* relationship for compounds **6a**,**c**,**d**,**f**,**g** 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 R^3 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 diatereoisomers **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** (R^3 = 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

(20) (a) Oppolzer, W.; Bättig, K. *Tetrahedron Lett.* **1982**, *23*, 4669. (b) Oppolzer, W.; Strauss, H. F.; Simmons, D. P. *Tetrahedron Lett.* **1982**, *23*, 4673. See also refs 1, 2, and 10.

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

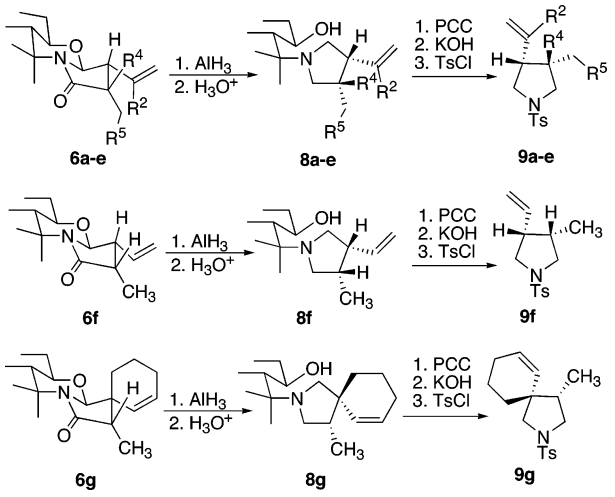
(22) Oppolzer clasified intramolecular ene reactions into type I, II, and III depending on the positioning of the bridge linking the enophile and the ene component. Later, Snider observed additional type IV ene reaction. (a) Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476.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

(23) (a) Mayer, C. F.; Crandall, J. K. *J. Org. Chem.* **1970**, *35*, 2688. (b) Iwasawa, N.; Takebayashi, T.; Mukaiyama, T. *Chem. Lett.* **1982**, 513. See also ref 2.

(24) See the Supporting Information.

(25) (a) Loncharich, R. J.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 6947. (b) Uchimaru, T.; Tsuzuki, S.; Tanabe, K.; Hayashi, Y. *J. Chem. Soc., Chem. Commun.* **1989**, 1861. (c) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556.

SCHEME 5



of the ene adducts with aluminum hydride in THF at −10 °C furnished the aminomenthol 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−H_2O 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 pyrrolidinones 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: CH_2Cl_2 from CaH_2 and THF and toluene from Na. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were registered in $CDCl_3$ 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 F_{254} indicator; the chromatograms were visualized under UV light and/or by staining with I_2 or phosphomolybdic acid. Flash chromatography was carried out on silica gel 60 (230−240 mesh).

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

(2*S*,4a*S*,7*R*,8a*R*)-2-Cyclohexen-1-yl-4,4,7-trimethyloctahydrobenz[*e*][1,3]oxazine (4). Colorless oil. $[\alpha]^{25}_D$ = +8.8 (*c* = 1.1, CH_2Cl_2). ^{1}H 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). ^{13}C 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 $C_{17}H_{29}NO$: C, 77.51; H, 11.10; N, 5.32. Found: C, 77.80; H, 10.96; N, 5.47.

(2*S*,4a*S*,7*R*,8a*R*)-*N*-Methacryloyl-2-(2-methylpropenyl)-4,4,7-trimethyloctahydrobenz[*e*][1,3]oxazine (5b). Colorless oil. $[\alpha]^{25}_D$ = +53.1 (*c* = 1.1, CH_2Cl_2). ^{1}H 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). ^{13}C 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 $C_{19}H_{31}NO_2$: C, 74.71; H, 10.23; N, 4.95. Found: C, 74.87; H, 10.38; N, 5.09.

(2*S*,4a*S*,7*R*,8a*R*)-*N*-Crotonyl-2-(2-methylpropenyl)-4,4,7-trimethyloctahydrobenz[*e*][1,3]oxazine (5c). Colorless oil. [a]$^{25}_D$ = +48.7 (*c* = 1.5, CH_2Cl_2). ^{1}H 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). ^{13}C 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 $C_{19}H_{31}NO_2$: C, 74.71; H, 10.23; N, 4.95. Found: C, 74.62; H, 10.34; N, 4.82.

(2*S*,4a*S*,7*R*,8a*R*)-*N*-Methacryloyl-2-(*trans*-2-phenylpropen-1-yl)-4,4,7-trimethyloctahydrobenz[*e*] [1,3]oxazine (5e). Colorless oil. $[\alpha]^{25}_D$ = +25.5 (*c* = 4.6, $CHCl_3$). ^{1}H NMR (δ): 0.88−1.20 (m, 3H); 0.89 (d, 3H, *J* = 6.5 Hz); 1.38−152 (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). ^{13}C 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 $C_{24}H_{33}NO_2$: C, 78.43; H, 9.05; N, 3.81. Found: C, 78.29; H, 9.17; N, 3.98.

(2*S*,4a*S*,7*R*,8a*R*)-*N*-Acryloyl-2-cyclohexen-1-yl-4,4,7-trimethyloctahydrobenz[*e*][1,3]oxazine (5g). Colorless oil. $[\alpha]^{25}_D$ = +52.9 (*c* = 1.7, $CHCl_3$). ^{1}H 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). ^{13}C NMR (δ): 19.0; 22.0; 22.2; 22.4; 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 $C_{20}H_{31}NO_2$: 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), K_2CO_3 (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*,3a*S*,4a*R*,6*R*,8a*S*)-3-Isopropenyl-2,6,9,9-tetramethyloctahydro-4a*H*-pyrrolo[2,1-*b*][1,3]benzoxazin-1(2*H*)-one (6a). Colorless solid. Mp: 92−93°C (from pentane). $[\alpha]^{25}_D$ = −173.5 (*c* = 1.0, CH_2Cl_2). ^{1}H 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). ^{13}C 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 $C_{18}H_{29}NO_2$: C, 74.18; H, 10.03; N, 4.81. Found: C, 74.31; H, 1018; N, 4.94.

(3*R*,3a*S*,4a*R*,6*R*,8a*S*)-3-Isopropenyl-2,2,6,9,9-pentamethyloctahydro-4a*H*-pyrrolo[2,1-*b*][1,3]benzoxazin-1(2*H*)-one (6b). Colorless solid. Mp: 126−127°C (from pentane). $[\alpha]^{25}_D = -116.0$ (c = 1.1, CH_2Cl_2). ^{1}H 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 $C_{19}H_{31}NO_2$: C, 74.71; H, 10.23; N, 4.59. Found: C, 74.62; H, 10.35; N, 4.73.

(2*S*,3*S*,3a*S*,4a*R*,6*R*,8a*S*)-3-Isopropenyl-2-ethyl-6,9,9-trimethyloctahydro-4a*H*-pyrrolo[2,1-*b*][1,3]benzoxazin-1(2*H*)-one (6c). Colorless solid. Mp: 89−90°C (from pentane). $[\alpha]^{25}_D = -146.1$ (c = 1.1, CH_2Cl_2). ^{1}H 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 $C_{19}H_{31}NO_2$: C, 74.71; H, 10.23; N, 4.59. Found: C, 74.84; H, 10.38; N, 4.71.

(3*R*,3a*S*,4a*R*,6*R*,8a*S*)-3-(1-Phenylvinyl)-2,2,6,9,9-pentamethyloctahydro-4a*H*-pyrrolo[2,1-*b*][1,3]benzoxazin-1(2*H*)-one (6e). Colorless solid. Mp: 163−164°C (from hexane). $[\alpha]^{25}_D = -16.4$ (c = 1.2, CH_2Cl_2). ^{1}H 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 $C_{24}H_{33}NO_2$: C, 78.43; H, 9.05; N, 3.81. Found: C, 78.28; H, 9.22; N, 3.65.

(2*S*,3*R*,3a*S*,4a*R*,6*R*,8a*S*)-2,6,9,9-Tetramethyl-3-vinyloctahydro-4a*H*-pyrrolo[2,1-*b*][1,3]benzoxazin-1(2*H*)-one (6f). Colorless oil. $[\alpha]^{25}_D = -97.9$ (c = 1.1, CH_2Cl_2). ^{1}H 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 $C_{17}H_{27}NO_2$: 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). $[\alpha]^{25}_D = -43.9$ (c = 1.0, $CHCl_3$). ^{1}H 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 $C_{20}H_{31}NO_2$: C, 75.67; H, 9.84; N, 4.41. Found: C, 75.83; H, 9.96; N, 4.54.

(2*R*,3*S*,3a*S*,4a*R*,6*R*,8a*S*)-2,6,9,9-Tetramethyl-3-vinyloctahydro-4a*H*-pyrrolo[2,1-*b*][1,3]benzoxazin-1(2*H*)-one (7f). Purity 90%. Colorless oil. ^{1}H 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). $[\alpha]^{25}_D = -99.0$ (c = 0.8, $CHCl_3$). ^{1}H 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 $C_{20}H_{31}NO_2$: C, 75.67; H, 9.84; N, 4.41. Found: C, 75.83; H, 10.01; N, 4.32.

(3*S*,4*S*)-*N*-(8-Mentholyl)-3-isoprenyl-4-methylpyrrolidine (8a). Yield: 87%. Colorless solid. Mp: 64−65°C (from AcOEt/hexane). $[\alpha]^{25}_D = -57.8$ (c = 1.1, CH_2Cl_2). ^{1}H 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 $C_{18}H_{33}NO$: C, 77.36; H, 11.90; N, 5.01. Found: C, 77.48; H, 12.03; N, 4.90.

(4*R*)-*N*-(8-Mentholyl)-4-isoprenyl-3,3-dimethylpyrrolidine (8b). Yield: 88%. Colorless oil. $[\alpha]^{25}_D = -21.1$ (c = 0.8, CH_2Cl_2). ^{1}H 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 $C_{19}H_{35}NO$: C, 77.76; H, 12.02; N, 4.77. Found: C, 77.60; H, 12.16; N, 4.59.

(3*S*,4*S*)-*N*-(8-Mentholyl)-3-ethyl-4-isopropenylpyrrolidine (8c). Yield: 90%. Colorless oil. $[\alpha]^{25}_D = -44.6$ (c = 1.0, CH_2Cl_2). ^{1}H 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 $C_{19}H_{35}NO$: C, 77.76; H, 12.02; N, 4.77. Found: C, 77.89; H, 11.91; N, 4.89.

(4*R*)-*N*-(8-Mentholyl)-3,3-dimethyl-4-(1-phenylvinyl)-pyrrolidine (8e). Yield: 96%. Colorless oil. $[\alpha]^{25}_D = +44.6$ (c = 0.9, CH_2Cl_2). ^{1}H 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). ^{13}C 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 $C_{24}H_{37}NO$: C, 81.07; H, 10.49; N, 3.94. Found: C, 81.18; H, 10.36; N, 4.17.

(3*R*,4*S*)-*N*-(8-Mentholyl)-3-methyl-4-vinylpyrrolidine (8f). Yield: 84%. Colorless solid. Mp: 59−60 °C (from AcOEt/hexane). $[\alpha]^{25}_D = -26.7$ (c = 1.0, CH_2Cl_2). ^{1}H 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). ^{13}C 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 $C_{17}H_{31}NO$: C, 76.92; H, 11.77; N, 5.28. Found: C, 77.07; H, 11.66; N, 5.37.

(4*S*,5*R*)-*N*-(8-Mentholyl)-4-methyl-2-azaspiro[4,5]dec-6-ene (8g). Yield: 85%. Colorless oil. $[\alpha]^{25}_D = -30.0$ (c = 1.2, $CHCl_3$). ^{1}H 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). ^{13}C 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 $C_{20}H_{35}NO$: C, 78.63; H, 11.55; N, 4.58. Found: C, 78.51; H, 11.67; N, 4.61.

(3*S*,4*S*)-*N*-Tosyl-3-isoprenyl-4-methylpyrrolidine (9a). Yield: 58%. Colorless solid. Mp: 55−56°C (from pentane). $[\alpha]^{25}_D = +10.8$ (c = 0.8, CH_2Cl_2). ^{1}H 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). ^{13}C 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 $C_{15}H_{21}NO_2S$: C, 64.48; H, 7.58; N, 5.01. Found: C, 64.59; H, 7.51; N, 4.90.

(4*R*)-*N*-Tosyl-4-isoprenyl-3,3-dimethylpyrrolidine (9b). Yield: 56%. Colorless oil. $[\alpha]^{25}_D = +5.0$ (c = 1.5, CH_2Cl_2). ^{1}H 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). ^{13}C 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 $C_{16}H_{23}NO_2S$: C, 65.49; H, 7.90; N, 4.77. Found: C, 65.63; H,;8.03 N, 4.82.

(3*S*,4*S*)-*N*-Tosyl-3-ethyl-4-isopropenylpyrrolidine (9c). Yield: 52%. Colorless oil. $[\alpha]^{25}_D = +11.5$ (c = 0.8, CH_2Cl_2). ^{1}H 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). ^{13}C 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 $C_{16}H_{23}NO_2S$: C, 65.49; H, 7.90; N, 4.77. Found: C, 65.52; H, 7.79; N, 4.65.

(4*R*)-*N*-Tosyl-3,3-dimethyl-4-(1-phenylvinyl)pyrrolidine (9e). Yield: 62%. Colorless oil. $[\alpha]^{25}_D = +73.4$ (c = 2.0, CH_2Cl_2). ^{1}H 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). ^{13}C 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 (2C); 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 $C_{21}H_{25}NO_2S$: C, 70.95; H, 7.09; N, 3.94. Found: C, 71.08; H, 6.98; N, 4.05.

(3*R*,4*S*)-*N*-Tosyl-3-methyl-4-vinylpyrrolidine (9f).[27] Yield: 50%. Colorless solid. Mp: 65−67 °C (from pentane). $[\alpha]^{25}_D = +9.3$ (c = 1.0, CH_2Cl_2). ^{1}H 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). ^{13}C NMR (δ): 13.5; 21.5; 36.5; 46.; 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 $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.23; H, 7.35; N, 5.26.

(4*S*,5*R*)-*N*-Tosyl-4-methyl-2-azaspiro[4,5]dec-6-ene (9g). Yield: 48%. Colorless oil. $[\alpha]^{25}_D = +39.4$ (c = 0.9, $CHCl_3$). ^{1}H 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). ^{13}C 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 $C_{17}H_{23}NO_2S$: C 66.85; H, 7.59; N, 4.59. Found: C, 66.79; H, 7.68; N, 4.31.

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Supporting Information Available: General experimental methods and copies of ^{1}H 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.

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(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.