Sequential Diastereoselective Addition of Allylic and Homoallylic Grignard Reagents to 2-Acyl-perhydro-1,3-benzoxazines and Ring-Closing Metathesis: an Asymmetric Route to Azepin-3-ol and Azocin-3-ol Derivatives

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Chiral 2-acyl-3-allyl-substituted perhydrobenzoxazines derived from (–)-8-aminomenthol react with allyl or homoallyl Grignard reagents to provide the corresponding tertiary alcohols in very good yields and with excellent diastereoselectivities. The 1,8- and 1,9-azadienes prepared in this way participate in RCM reactions to give good yields of seven- and eight-membered nitrogen heterocycles. The yields of the RCM reaction increased when the hydrochlorides were used instead of the neutral azadienes. The removal of the chiral adjuvant allowed the preparation of enantiopure azepin-3-ol and azocin-3-ol derivatives.

Introduction

Seven- and eight-membered nitrogen heterocycles are an important class of compounds with applications in natural products chemistry and pharmaceutical research[1] and so are popular targets for synthetic chemistry. However, cyclization reactions affording medium-ring heterocycles are often slow and hampered by unfavorable enthalpies and entropies of reaction, especially in the case of eight-membered rings.[2] Accordingly, relatively few methods for their preparation are available.

The tremendous growth in the area of transition metal-mediated synthetic methodology in the past decade[3] has allowed the development of new cyclization strategies for medium-sized rings.[4] In this context, the ring-closing metathesis (RCM) reaction catalyzed by metal alkylidene complexes has emerged as a powerful tool for the preparation of carbo- and heterocycles from acyclic diene precursors,[5,6] including nitrogen heterocycles[7,8] and medium-sized rings.[9]

Chiral perhydro-1,3-benzoxazines derived from (–)-8-aminomenthol[10] have been shown to be useful in cyclization reactions affording enantiopure nitrogen heterocycles,[11] and we now report on the synthesis of enantiopure 2,3,4,7-tetrahydro-1*H*-azepin-3-ols and 1,2,3,4,5,8-hexahydroazocin-3-ols with the aid of this template. The methodology is based on the sequential diastereoselective addition of allylic or homoallylic Grignard reagents to *N*-allyl-2-acylperhydro-1,3-benzoxazines and subsequent RCM. In this way, the chiral perhydrobenzoxazine furnishes the environment necessary for the diastereoselective transformations and introduces a cyclic conformational constraint that greatly enhances the ability of dienes to undergo RCM to afford eight-membered rings.[12,13]

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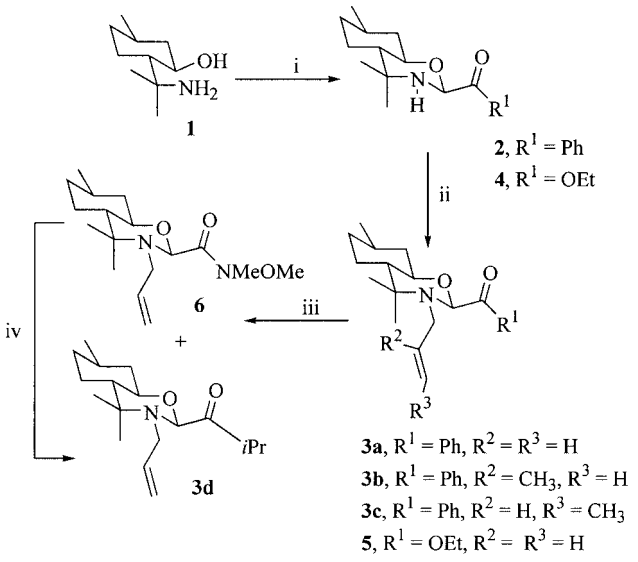
Results and Discussion

The preparation of the starting 2-benzoyl-perhydro-1,3-benzoxazines **3a**–**c** was accomplished in two steps from (–)-8-aminomenthol (**1**; Scheme 1). Condensation of **1** with phenylglyoxal quantitatively afforded **2**, which was alkylated with allylic bromides in the presence of potassium carbonate in acetonitrile at reflux[14] to give **3a**–**c**.

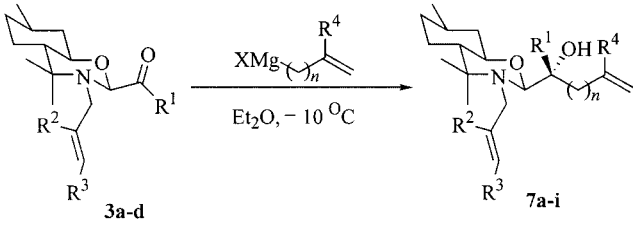
Treatment of **1** with ethyl glyoxylate ethyl hemiacetal yielded **4**, which was alkylated with allyl bromide to give **5**. This was transformed into a mixture of Weinreb amide **6** (49%) and isopropyl ketone **3d** (36%) by treatment with *N*,*O*-dimethylhydroxylamine hydrochloride and isopropylmagnesium chloride in THF at –10 °C.[15] Treatment of isolated **6** with isopropylmagnesium chloride in THF at –40 °C yielded further **3d** in 88% yield (80% total yield from **5**).

As would be expected,[16] treatment of allylic and homoallylic Grignard reagents with the chiral 2-acyl-perhydro-1,3-benzoxazines **3a**–**d** provided good chemical yields and excellent diastereoselection. The reactions were carried out in ether at –10 °C with excesses of Grignard reagent, and alcohols (**7a**–**i**) were obtained as single diastereomers or with good diastereomeric excesses (*de*) (Scheme 2 and Table 1).

The absolute configurations at the newly created stereocenters were assigned as *S* in agreement with Eliel's re-



Scheme 1. Reagents and conditions: I) HOCCOPh or HO(EtO)CHCO$_2$Et, CH_2Cl_2, room temp., quant. ii) allyl bromides, K_2CO_3, acetonitrile, reflux, **3a** (90%), **3b** (80%), **3c** (88%), **5** (85%). iii) MeNHOMe·HCl, *i*PrMgCl, THF, –10 °C to room temperature, **6** (49%), **3d** (36%). iv) *i*PrMgCl, THF, –40 °C **3d** (88%).



Scheme 2.

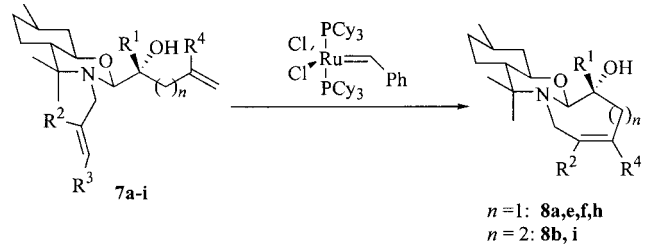
ports[16] and confirmed on the RCM product for **7e** (vide infra).

All major diastereoisomers formed in each reaction were isolated and purified by flash chromatography and/or crystallization, and were then subjected to ring-closing metathesis. The first-generation ruthenium(II) complex bis-(tricyclohexylphosphane)benzylideneruthenium dichloride was used as the catalyst precursor and the reactions were carried out under dilute conditions (0.01 M) to avoid competition with dimerization. The results are summarized in Scheme 3 and Table 2.

Table 1. Reagents used to provide 2-acyloxazines **3a**–**d**.

Entry	R^1	R^2	R^3	R^4	*n*	Yield (%)[a]	*de*[b]
1	Ph	H	H	H	1	**7a** (89)	90
2	Ph	H	H	H	2	**7b** (92)	>95[c]
3	Ph	H	CH_3	H	1	**7c** (90)	92
4	Ph	H	CH_3	H	2	**7d** (85)	>95[c]
5	Ph	CH_3	H	H	1	**7e** (89)	92
6	Ph	H	H	CH_3	1	**7f** (80)	86
7	Ph	CH_3	H	H	2	**7g** (82)	>95[c]
8	*i*Pr	H	H	H	1	**7h** (90)	90
9	*i*Pr	H	H	H	2	**7i** (83)	>95[c]

[a] Yield refers to isolated major diastereoisomer after column chromatography. [b] Diastereomeric excesses were determined by integration of the ^{1}H NMR signals of the reaction mixtures. [c] Only one diastereoisomer was detected by ^{1}H NMR spectroscopy.



Scheme 3.

Initial experiments were conducted on perhydro-1,3-benzoxacine **7a** with monosubstituted olefinic appendages. Reactions were carried out in CH_2Cl_2 at room temperature,

Table 2. Ring-closing metathesis reaction of dienes 7**a**–**i**.

Entry	Compound	Solvent	*T* (°C)	Catalyst mol-%[a]	Time (h)[a]	Yield (%)[b]
1	**7a**	CH_2Cl_2	20	4	20	**8a** (40)[d]
2	**7a**	CH_2Cl_2	20	4 + 4	20 + 10	**8a** (80)[d]
3	**7a**	CH_2Cl_2	reflux	4 + 4	10 + 10	**8a** (90)
4	**7b**	CH_2Cl_2	reflux	4 + 4 + 4	10 + 10 + 10	**8b** (56)[d]
5	**7b**	C_6H_6	reflux	4 + 4 + 4	10 + 10 + 10	**8b** (68)[d]
6	**7b**	CH_2Cl_2	20	8 + 4[c]	10 + 10	**8b** (15)[d]
7	**7c**	CH_2Cl_2	reflux	4 + 4	10 + 18	**8a** (90)
8	**7d**	C_6H_6	reflux	4 + 4 + 4	20 + 10 + 10	**8b** (48)[d]
9	**7a**·HCl	CH_2Cl_2	20	3	15	**8a** (95)
10	**7b**·HCl	CH_2Cl_2	20	3 + 2	25 + 20	**8b** (80)[d]
11	**7c**·HCl	CH_2Cl_2	20	3	15	**8a** (93)
12	**7d**·HCl	CH_2Cl_2	20	3 + 3	25 + 20	**8b** (70)[d]
13	**7e**·HCl	CH_2Cl_2	20	3 + 3	25 + 20	**8e** (92)
14	**7f**·HCl	CH_2Cl_2	reflux	3 + 4 + 4 + 4	30 + 60 + 60 + 90	**8f** (67)[d]
15	**7g**·HCl	CH_2Cl_2	reflux	3 + 4 + 5	30 + 40 + 40	–
16	**7h**·HCl	CH_2Cl_2	20	3	15	**8h** (92)
17	**7i**·HCl	CH_2Cl_2	20	3 + 2	30 + 40	**8i** (81)[d]

[a] Catalyst was replenished after the time indicated in the Table; see also Experimental Section. [b] Yields refer to pure compounds after column chromatography. [c] An additional 30 mol-% of Ti(O*i*Pr)$_4$ was added. [d] Different amounts of the starting materials were recovered.

and 4 mol-% of the first-generation Grubbs' catalyst was used. Under these conditions azepine **8a** was formed after 20 h of reaction but only in 40% yield. The yield was increased to 80% if 8 mol-% of catalyst was used, and to 90% when the mixture was heated to reflux (Entries 1–3 in Table 2). In contrast, the formation of the eight-membered heterocycle was more difficult, and azocine **8b** was isolated in only 56% yield from 7b even with 12 mol-% of catalyst in dichloromethane. A change to benzene at reflux as solvent caused a moderate increase in the yield, up to 68% (Entries 4, 5 in Table 2).

The moderate yield in the formation of the eight-membered ring compound **8b** could be due to coordination of the nitrogen atom of the perhydro-1,3-benzoxazine to the ruthenium catalyst, resulting in deactivation of the metal complex through heteroatom–metal chelation.[17–19] This problem has been solved elsewhere by addition of substoichiometric amounts of $Ti(OiPr)_4$, which competes with the nitrogen atom, avoiding the formation of unreactive chelates.[20] In our case, though, addition of 30 mol-% of the titanate to the reaction mixture only cause extensive decomposition of **7b**.

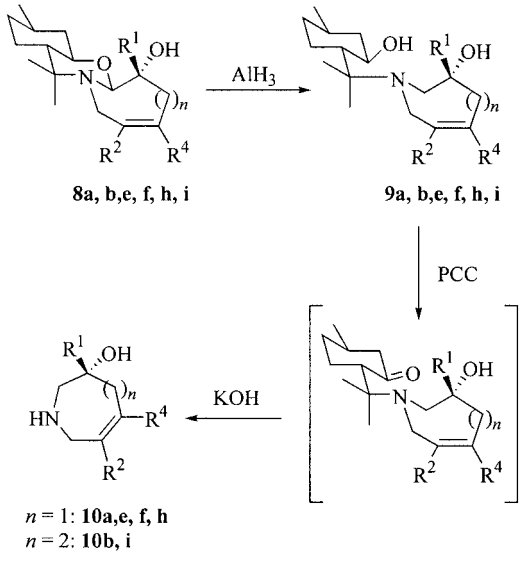
Because metathesis of monosubstituted olefins is known to be more rapid than that of disubstituted olefins, we tested the metathesis reaction in derivatives **7c** and **7d** (Entries 7 and 8) with a crotylamine and an allylamine instead, to ensure that the catalyst would react first with the terminal alkene more distant from the nitrogen atom and to disfavor formation of the undesired intermediates.[21] In this way, azepine **8a** was obtained from **7c** in a similar chemical yield to that obtained from **7a** (compare Entries 3 and 7), but the eight-membered azocine **8b** was formed in lower yield from **7d** than from **7b** (compare Entry 5 vs. 8).

Finally we tested the protonation of perhydrobenzoxazines to block the basic nitrogen functionality.[22,23] This was easily achieved by bubbling gaseous hydrochloric acid into ethereal solutions of **7a**–**i**, followed by removal of the solvent under vacuum. Treatment of the hydrochloride salt of **7a** in CH_2Cl_2 at room temperature with only 3 mol-% of Grubbs' catalyst, followed by a basic workup, gave the desired azepine **8a** in an excellent 95% yield (Entry 9). Azocine **8b** was obtained in 80% yield from the hydrochloride salt of **7b** with the use of 5 mol-% of catalyst (Entry 10). Similar results were obtained for azepine **8h** and azocine **8i**, with an isopropyl group instead of a phenyl group (Entries 16 and 17). Moreover, when starting from the hydrochloride salts of the crotyl derivatives **7c** and **7d**, azepine **8a** was also isolated in excellent yield (Entry 11) but azocine **8b** was isolated only in 70% yield (Entry 12).

Azepines with trisubstituted double bonds were also formed under these conditions.[24] Azepine **8e** was prepared in 92% yield from the hydrochloride salt of methallyl derivative **7e** by use of 6 mol-% of catalyst (Entry 13), whereas formation of azepine **8f**, also with a trisubstituted double bond, required up to 15 mol-% of catalyst and heating at reflux in CH_2Cl_2 for 240 h to provide a 67% chemical yield (Entry 14). Under these conditions, moreover, an 18% yield of the *N*-unsubstituted oxazine resulting from deprotection of the tertiary allylic amine[25,26] was isolated. The reason for the difference in reactivity between the hydrochloride salts of **7e** and **7f** is unclear,[27] although the higher reactivity of **7e** may be due to better adoption of a conformation more favorable for cyclization.

Nevertheless it was not possible to obtain azocines with a trisubstituted double bond under these conditions. The attempted RCM reaction of the hydrochloride salt of **7g** only gave starting material, together with variable amounts of products identified as dimers resulting from intermolecular cross-metathesis (Entry 15). The second-generation Grubbs' catalyst $(IMes)(PCy_3)(Cl_2)Ru{=}CHPh$ also failed to give the corresponding azocine. The only cyclized product obtained in this reaction was the azepine **7e** (32%), the result of a double bond isomerization[26] prior to the RCM, and dimeric products.

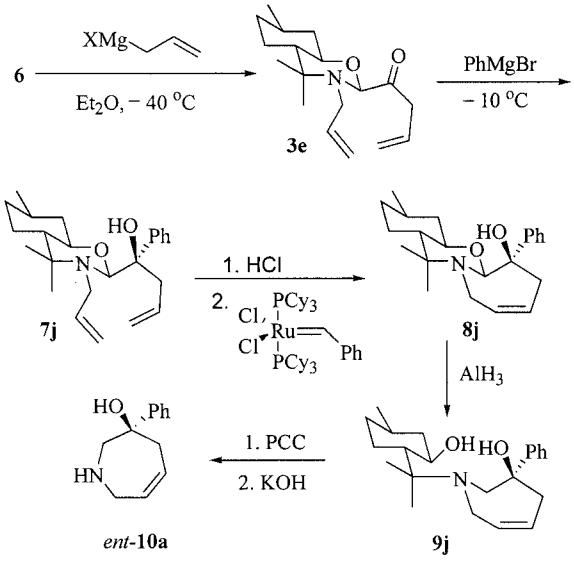
Transformation of compounds **8a**, **8e**, **8f**, and **8h** into the final enantiopure 2,3,4,7-tetrahydro-1*H*-azepin-3-ols **10a**, **10e**, **10f**, and **10h**, respectively, and of **8b** and **8i** into the enantiopure 1,2,3,4,5,8-hexahydroazocin-3-ols **10b** and **10i** was performed in two steps,[28] as depicted in Scheme 4. The reductive ring-opening of the N,O-acetal moiety by treatment of **8a**, **8b**, **8e**, **8f**, **8h**, or **8i** with aluminium hydride in THF at reflux for 10 min gave the amino alcohols **9a**, **9b**, **9e**, **9f**, **9h**, or **9i** in very good yields. At this point, the stereochemistry of compound **9e** was determined by X-ray diffraction analysis,[29] corroborating the configurations of the quaternary carbinol stereocenters created by addition of the Grignard reagents to the perhydrobenzoxazines **3a**–**d**. Upon oxidation with PCC in CH_2Cl_2 at room temperature these aminomenthol derivatives gave the corresponding aminomenthone derivatives, which were treated, without isolation, with 2.5 M aqueous KOH in THF/methanol to furnish the final azepin-3-ol (**10a**, **10e**, **10f**, **10h**) and azocin-3-ol (**10b**, **10i**) derivatives in 44–56% yields from **8a**–**i**.



Scheme 4.

We assume that the epimerization of the newly created stereocenters is very difficult in the transformations of **8a**–

i into the final products **10a**–**i**, and consequently that these should be enantiopure compounds. To test the stereochemical purity, *ent*-**10a** was prepared as summarized in Scheme 5. Allyl ketone **3e** was obtained (70%) by reaction of Weinreb amide **6** with allylmagnesium bromide, and was transformed into the homoallylic alcohol **7j** (92%, *de* > 96%) by treatment with phenylmagnesium bromide. After treatment with anhydrous HCl, compound **7j** was transformed into the azepine derivative **8j** in 90% yield under the general conditions described for the RCM reaction. The reductive ring-opening to **9j** and removal of the menthol appendage yielded *ent*-**10a** in 50% yield from **8j**. This compound showed identical physical and spectroscopic properties and nearly the same optical rotation (with opposite sign) as **10a**. Unfortunately, we were unable to differentiate the two enantiomers by chiral HPLC under different conditions (Chiralcel OD column 0.46×25 cm and hexane/2-propanol mixtures as eluent)



Scheme 5.

In summary, the synthetic sequence described above constitutes a useful procedure for the preparation of enantiopure 2,3,4,7-tetrahydro-1*H*-azepin-3-ols and 1,2,3,4,5,8-hexahydroazocin-3-ols. Although 1,9-azadienes are relatively poor substrates for RCM,[9] the efficient cyclization in our reagents is probably due to the perhydrobenzoxazine moiety to which the reacting alkenes are tethered.[30]

To this end we also prepared the enantiomer of compound **10a** and we studied their separation by HPLC after coinjection with the described compound. Unfortunately, we have been unable to find conditions for a good separation and so cannot determine the enantiopurity in the final products.

On the other hand, the authors disagree in part with the comment of one referee, because, once the diastereomeric purities for compounds **8a**–**i** are established, the conditions used for their transformation into the final derivatives **10a**–**i** allow the conservation of their stereochemical integrity.

Experimental Section

General Methods: All reactions were carried out under argon in oven-dried glassware. Solvents were dried by standard methods: CH_2Cl_2 was distilled from CaH_2, acetonitrile from P_2O_5, and THF and benzene from sodium. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were registered in $CDCl_3$ as solvent, and chemical shifts are reported relative to tetramethylsilane as internal reference. Specific rotations were determined on a digital polarimeter with 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 F_{254} indicator, the chromatograms were viewed 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 **2**, **4**, **3c**, and **3a** have been described previously.[14]

Synthesis of Perhydrobenzoxazines 3a–c and 5: A mixture of benzoxazine **2** or **4** (20 mmol), potassium carbonate (3.9 g, 28 mmol), and the appropriate allylic bromide (28 mmol) in acetonitrile (8 mL) was heated in an oil bath at 80–90 °C until the reaction was complete (TLC, 60–80 h). The reaction mixture was diluted with ethyl acetate, and the solid was separated by filtration and washed with hot ethyl acetate (3×25 mL). The solvents were evaporated under vacuum and the residue was purified by flash chromatography on silica gel with hexanes/ethyl acetate 1:30 as eluent for **3a**–**c** and 1:50 for **5**.

[[2*S*(2α,4aα,7α,8aβ)]-4,4,7-Trimethyl-3-(2-methylallyl)-octahydrobenzo[*e*][1,3]oxazin-2-yl]phenyl-methanone (3b): Colorless solid. M.p.: 84–85 °C (from EtOH). $[\alpha]_D^{25}$ = –14.1 (*c* = 1.0, CH_2Cl_2). ^1H NMR: δ = 0.92–1.09 (m, 2 H), 0.95 (d, *J* = 6.5 Hz, 3 H), 1.15 (s, 3 H), 1.26 (m, 1 H), 1.34 (s, 3 H), 1.46 (s, 3 H), 1.48–1.69 (m, 3 H), 1.73 (m, 1 H), 2.03 (m, 1 H), 3.16 (d, *J* = 17.8 Hz, 1 H), 3.28 (d, *J* = 17.8 Hz, 1 H), 3.62 (td, J_1 = 10.5, J_2 = 4.0 Hz, 1 H), 4.40 (d, *J* = 0.8 Hz, 1 H), 4.63 (d, *J* = 0.8 Hz, 1 H), 5.89 (s, 1 H), 7.39 (m, 2 H), 7.48 (m, 1 H), 8.10 (m, 2 H) ppm. ^{13}C NMR: δ = 20.1, 20.6, 22.1, 24.8, 26.1, 31.2, 34.8, 41.0, 45.2, 49.2, 57.9, 76.4, 87.4, 111.4, 127.7 (2 C), 129.1 (2 C), 132.7, 135.2, 144.1, 194.6 ppm . IR (nujol dispersion): $\tilde{\nu}$ = 3080, 1700, 1600, 780, 690 cm^{-1}. $C_{22}H_{31}NO_2$ (341.49): C 77.38, H 9.15, N 4.10; found C 77.52, H 9.29, N 4.00.

Ethyl [2*S*(2α,4aα,7α,8aβ)]-3-Allyl-4,4,7-trimethyl-octahydrobenzo-[*e*][1,3]oxazine-2-carboxylate (5): Colorless oil. $[\alpha]_D^{25}$ = –40.2 (*c* = 1.1, CH_2Cl_2). ^1H NMR: δ = 0.90–1.04 (m, 2 H), 0.92 (d, *J* = 6.5 Hz, 3 H), 1.17 (s, 3 H), 1.22 (m, 1 H), 1.23 (s, 3 H), 1.27 (dd, J_1 = 7.5, J_2 = 7.0 Hz, 3 H), 1.40–1.53 (m, 2 H), 1.61 (m, 1 H), 1.70 (m, 1 H), 1.97 (m, 1 H), 3.28 (dd, J_1 = 17.5, J_2 = 5.7 Hz, 1 H), 3.39 (dd, J_1 = 17.5, J_2 = 5.7 Hz, 1 H), 3.50 (td, J_1 = 10.6, J_2 = 4.1 Hz, 1 H), 4.06–4.27 (m, 2 H), 4.95 (dd, J_1 = 10.3, J_2 = 1.7 Hz, 1 H), 5.10 (s, 1 H), 5.11 (dd, J_1 = 17.2, J_2 = 1.7 Hz, 1 H), 5.83 (m, 1 H) ppm. ^{13}C NMR: δ = 13.9, 20.2, 22.0, 24.8, 26.3, 31.2, 34.8, 40.9, 45.7, 47.0, 57.2, 61.0, 76.0, 85.3, 114.2, 139.0, 169.0 ppm. IR (film): $\tilde{\nu}$ = 3080, 1760, 1645, 740 cm^{-1}. $C_{17}H_{29}NO_3$ (295.42): C 69.12, H 9.89, N 4.74; found C 69.26, H 9.96, N 4.88.

Synthesis of Benzoxazine 3d: A solution of *i*PrMgCl in diethyl ether (10.5 mL, 2 M) was slowly added (2 h) to a slurry of the ester **5** (1.5 g, 5.08 mmol) and Me(MeO)NH·HCl (0.74 g, 7.62 mmol) in THF (25 mL), cooled to –10 °C. The mixture was stirred for 10 min at –10 °C and then for 15 min at room temperature. The reaction was quenched with a saturated solution of NH_4Cl, and the product was extracted with diethyl ether (4×20 mL). The organic layer was dried over $MgSO_4$ and concentrated under vacuum to give an oily residue, which was purified by flash chromatography on silica gel

with hexanes/ethyl acetate as eluent to yield 0.78 g of amide **6** and 0.54 g of ketene **3d**.

A solution of *i*PrMgCl (2 mL, 2 M) was slowly added at –40 °C to a solution of amide **6** in THF (8 mL) . The reaction mixture was stirred for 30 min and the mixture was treated as above to obtain 0.65 g of ketone **3d**.

[2*S*(2α,4aα,7α,8aβ)]-3-Allyl-*N*-methoxy-*N*,4,4,7-tetramethyl-octahydrobenzo[*e*][1,3]oxazine-2-carboxamide (6): Colorless oil. $[\alpha]_D^{25}$ = –42.7 (*c* = 0.9, CH_2Cl_2). ^1H NMR: δ = 0.85–1.07 (m, 2 H), 0.92 (d, *J* = 6.4 Hz, 3 H), 1.17 (s, 3 H), 1.20 (m, 1 H), 1.27 (s, 3 H), 1.38–1.54 (m, 2 H), 1.58 (m, 1 H), 1.70 (m, 1 H), 1.96 (m, 1 H), 3.12 (s, 3 H), 3.17–3.78 (m, 3 H), 3.80 (s, 3 H), 4.89 (d, *J* = 10.1 Hz, 1 H), 5.02 (d, *J* = 17.3 Hz, 1 H), 5.63 (s, 1 H), 5.84 (m, 1 H) ppm. ^{13}C NMR: δ = 21.0, 22.0, 24.7, 26.5, 31.1, 32.0, 34.7, 40.9, 45.2, 46.1, 57.4, 61.4, 76.5, 82.0, 113.6, 139.7, 169.5 ppm. IR (film): $\tilde{\nu}$ = 3070, 1680, 735, 700 cm^{-1}. $C_{17}H_{30}N_2O_3$ (310.43): C 65.77, H 9.74, N 9.02; found C 65.92, H 9.64, N 9.11.

1-[[2*S*(2α,4aα,7α,8aβ)]-3-Allyl-4,4,7-trimethyl-octahydrobenzo[*e*]-[1,3]oxazin-2-yl]-2-methylpropan-1-one (3d): Colorless oil. $[\alpha]_D^{25}$ = –67.4 (*c* = 1.1, CH_2Cl_2). ^1H NMR: δ = 0.85–1.21 (m, 3 H), 0.92 (d, *J* = 6.6 Hz, 3 H), 1.03 (d, *J* = 6.8 Hz, 3 H), 1.11 (d, *J* = 7.1 Hz, 3 H), 1.15 (s, 3 H), 1.27 (s, 3 H), 1.38–1.43 (m, 2 H), 1.61 (m, 1 H), 1.71 (m, 1 H), 1.96 (m, 1 H), 3.04–3.15 (m, 2 H), 3.32 (dd, J_1 = 17.8, J_2 = 5.0 Hz, 1 H), 3.48 (td, J_1 = 10.6, J_2 = 4.0 Hz, 1 H), 4.96 (dd, J_1 = 10.3, J_2 = 1.7 Hz, 1 H), 5.08 (dd, J_1 = 17.2, J_2 = 1.7 Hz, 1 H), 5.19 (s, 1 H), 5.81 (m, 1 H) ppm. ^{13}C NMR: δ = 17.2, 19.3, 21.4, 22.0, 24.8, 26.4, 31.2, 34.8, 36.1, 41.0, 44.8, 47.3, 57.3, 76.3, 88.0, 114.2, 139,5, 210.5 ppm. IR (film): $\tilde{\nu}$ = 3060, 1730, 735, 690 cm^{-1}. $C_{18}H_{31}NO_2$ (293.44): C 73.67, H 10.65, N 4.77; found C 73.54, H 10.79, N 4.70.

1-[[2*S*(2α,4aα,7α,8aβ)]-3-Allyl-4,4,7-trimethyl-octahydrobenzo[*e*]-[1,3]oxazin-2-yl]but-3-en-1-one (3e): Colorless oil. $[\alpha]_D^{25}$ = –62.1 (*c* = 0.6, CH_2Cl_2). ^1H NMR: δ = 0.84–1.1 (m, 2 H), 0.93 (d, *J* = 6.5 Hz, 3 H), 1.11 (m, 1 H), 1.15 (s, 3 H), 1.20 (s, 3 H), 1.39–1.50 (m, 2 H), 1.63 (m, 1 H), 1.69 (m, 1 H), 1.96 (m, 1 H), 3.09–3.21 (m, 2 H), 3.37 (dt, J_1 = 7.0, J_2 = 1.3 Hz, 2 H), 3.46 (td, J_1 = 10.6, J_2 = 4.1 Hz, 1 H), 4.93 (s, 1 H), 4.94–5.19 (m, 4 H), 5.72–6.0 (m, 2 H) ppm. ^{13}C NMR: δ = 19.8, 22.2, 24.9, 26.5, 31.3, 34.8, 41.1, 43.6, 46.0, 47.1, 57.4, 75.9, 89.6, 115.0, 118.7, 130.6, 138.9, 205.4 ppm. IR (film): $\tilde{\nu}$ = 3078, 1730, 1455, 915 cm^{-1}. $C_{18}H_{29}NO_2$: C 74.18, H 10.03, N 4.81; found C 74.32, H 10.19, N 4.95.

Diastereoselective Addition of Allylic and Homoallylic Grignard Reagents to 6a–d: A solution of the appropriate freshly prepared allyl- or homoallylmagnesium bromide derivative[31] (13 mL, 1 M) in ether was slowly added at –10 °C to a solution of the appropriate benzoxazine **6a**–**d** (6.0 mmol) in diethyl ether (30 mL). The mixture was stirred at this temperature until disappearance of the starting material (TLC, 15–45 min.). The reaction mixture was quenched with saturated ammonium chloride, and the product was extracted with diethyl ether (3×25 mL). The organic extracts were washed with brine and dried over anhydrous $MgSO_4$, and the solvent was evaporated in vacuo. The residue was chromatographed on silica gel with hexanes/ethyl acetate 1:70 as eluent.

(1*S*)-1-[[2*S*(2α,4aα,7α,8aβ)]-3-Allyl-4,4,7-trimethyl-octahydrobenzo-[*e*][1,3]oxazin-2-yl]-1-phenylbut-3-en-1-ol (7a): Colorless oil. $[\alpha]_D^{25}$ = –5.6 (*c* = 0.9, CH_2Cl_2). ^1H NMR: δ = 0.83–1.00 (m, 2 H), 0.94 (s, 3 H), 0.95 (d, *J* = 6.5 Hz, 3 H), 1.12 (m, 1 H), 1.22 (s, 3 H), 1.46–1.57 (m, 3 H), 1.70 (m, 1 H), 1.95 (m, 1 H), 2.49 (ddt, J_1 = 13.6, J_2 = 7.0, J_3 = 1.3 Hz, 1 H), 2.68 (ddt, J_1 = 13.6, J_2 = 7.2, J_3 = 1.3 Hz, 1 H), 3.08 (dd, J_1 = 17.5, J_2 = 6.7 Hz, 1 H), 3.14 (s, 1 H), 3.61 (td, J_1 = 10.5, J_2 = 4.0 Hz, 1 H), 3.75 (m, 1 H), 4.47 (dq, J_1 = 10.1, J_2 = 1.3 Hz, 1 H), 4.56 (dq, J_1 = 17.5, J_2 = 1.3 Hz, 1 H), 4.84 (m, 1 H), 4.90–4.97 (m, 2 H), 4.95 (s, 1 H), 5.56 (m, 1 H), 7.19 (m, 1 H), 7.28 (m, 2 H), 7.35 (m, 2 H) ppm. ^{13}C NMR: δ = 22.3, 22.4, 25.0, 26.9, 31.5, 35.2, 41.6, 44.9, 46.3, 49.6, 57.9, 77.4, 77.1, 89.3, 111.5, 117.6, 126.0, 126.3 (2 C), 127.1 (2 C), 134.0, 142.3 (2 C) ppm. IR (film): $\tilde{\nu}$ = 3530 (broad), 3060, 1630, 1595, 760, 710, 695, 670 cm^{-1}. $C_{24}H_{35}NO_2$ (369.54): C 78.00, H 9.55, N 3.79; found C 78.16, H 9.71, N 3.67.

(1*S*)-1-[[2*S*(2α,4aα,7α,8aβ)]-3-Allyl-4,4,7-trimethyl-octahydrobenzo-[*e*][1,3]oxazin-2-yl]-1-phenyl-pent-4-en-1-ol (7b): Colorless solid. M.p.: 71–72 °C (from EtOH). $[\alpha]_D^{25}$ = –12.9 (*c* = 1.0, CH_2Cl_2). ^1H NMR: δ = 0.83–1.03 (m, 2 H), 0.92 (s, 3 H), 0.95 (d, *J* = 6.5 Hz, 3 H), 1.12 (m, 1 H), 1.22 (s, 3 H), 1.45–1.61 (m, 4 H), 1.66–1.76 (m, 2 H), 1.96 (m, 1 H), 2.01–2.16 (m, 2 H), 3.05 (s, 1 H), 3.06 (dd, J_1 = 17.5, J_2 = 6.7 Hz, 1 H), 3.62 (td, J_1 = 10.5, J_2 = 4.0 Hz, 1 H), 3.76 (m, 1 H), 4.45 (d, J_1 = 10.1 Hz, 1 H), 4.55 (d, *J* = 17.2 Hz, 1 H), 4.64 (m, 1 H), 4.82–4.92 (m, 2 H), 4.90 (s, 1 H), 5.70 (m, 1 H), 7.18 (m, 1 H), 7.28 (m, 2 H), 7.34 (m, 2 H) ppm. ^{13}C NMR: δ = 22.3, 22.4, 24.9, 26.9, 27.5, 31.4, 35.1, 41.5, 43.9, 44.7, 46.1, 57.7, 77.2, 77.4, 90.3, 111.3, 113.8, 125.8, 126.2 (2 C), 127.1 (2 C), 139.1, 142.0, 142.3 ppm. IR (nujol dispersion): $\tilde{\nu}$ = 3535 (broad), 3055, 1630, 1595, 758, 695 cm^{-1}. $C_{25}H_{37}NO_2$ (383.57): C 78.28, H 9.72, N 3.65; found C 78.41, H 9.60, N 3.54.

(1*S*)-1-[[2*S*(2α,4aα,7α,8aβ)]-3-(But-2-enyl)-4,4,7-trimethyl-octahydrobenzo[*e*][1,3]oxazin-2-yl]-1-phenylbut-3-en-1-ol (7c): Colorless oil. $[\alpha]_D^{25}$ = +17.3 (*c* = 1.2, CH_2Cl_2). ^1H NMR: δ = 0.82–1.04 (m, 2 H), 0.94 (s, 3 H), 0.95 (d, *J* = 6.5 Hz, 3 H), 1.12 (m, 1 H), 1.21 (s, 3 H), 1.35 (dd, J_1 = 6.1, J_2 = 1.0 Hz, 3 H), 1.38–1.68 (m, 3 H), 1.71 (m, 1 H), 1.95 (m, 1 H), 2.49 (dd, J_1 = 13.6, J_2 = 7.0 Hz, 1 H), 2.68 (dd, J_1 = 13.6, J_2 = 7.4 Hz, 1 H), 3.02 (dd, J_1 = 17.1, J_2 = 6.3 Hz, 1 H), 3.15 (s, 1 H), 3.61 (m, 2 H), 4.49 (m, 1 H), 4.87–4.98 (m, 3 H), 4.94 (s, 1 H), 5.57 (m, 1 H), 7.20 (m, 1 H), 7.28 (m, 2 H), 7.35 (m, 2 H) ppm. ^{13}C NMR: δ = 17.6, 22.3 (2 C), 24.9, 26.6, 31.4, 35.2, 41.6, 44.9, 45.0, 49.4, 57.6, 76.9, 77.3, 89.3, 117.5, 122.0, 125.8, 126.2 (2 C), 126.9 (2 C), 134.0, 134.3, 142.2 ppm. IR (film): $\tilde{\nu}$ = 3550 (broad), 3070, 1640, 1605, 765, 710, 700, 675 cm^{-1}. $C_{25}H_{37}NO_2$ (383.57): C 78.28, H 9.72, N 3.65; found C 78.19, H 9.61, N 3.80.

(1*S*)-1-[[2*S*(2α,4aα,7α,8aβ)]-3-(But-2-enyl)-4,4,7-trimethyl-octahydrobenzo[*e*][1,3]oxazin-2-yl]-1-phenylpent-4-en-1-ol (7d): Colorless solid. M.p.: 98–99 °C (from hexane). $[\alpha]_D^{25}$ = –5.5 (*c* = 0.9, CH_2Cl_2). ^1H NMR: δ = 0.85–1.02 (m, 2 H), 0.93 (s, 3 H), 0.94 (d, *J* = 6.6 Hz, 3 H), 1.10 (m, 1 H), 1.20 (s, 3 H), 1.34 (dd, J_1 = 6.5, J_2 = 1.0 Hz, 3 H), 1.41–1.63 (m, 4 H), 1.65–1.78 (m, 2 H), 1.95 (m, 1 H), 2.03–2.17 (m, 2 H), 3.00 (dd, J_1 = 17.3, J_2 = 6.6 Hz, 1 H), 3.06 (s, 1 H), 3.55–3.65 (m, 2 H), 4.43 (m, 1 H), 4.79–4.96 (m, 3 H), 4.89 (s, 1 H), 5.70 (m, 1 H), 7.18 (m, 1 H), 7.27 (m, 2 H), 7.34 (m, 2 H) ppm. ^{13}C NMR: δ = 17.6, 22.3, 22.4, 25.0, 26.7, 27.5, 31.5, 35.2, 41.6, 43.9, 45.0 (2 C), 57.6, 76.6, 77.3, 90.5, 113.8, 122.0, 125.8, 126.3 (2 C), 127.1 (2 C), 134.4, 139.3, 142.3 ppm. IR (nujol dispersion): $\tilde{\nu}$ = 3545 (broad), 3075, 3030, 1640, 1600, 765, 700, 650 cm^{-1}. $C_{26}H_{39}NO_2$ (397.59): C 78.54, H 9.89, N 3.52; found C 78.42, H 10.02, N 3.66.

(1*S*)-1-[[2*S*(2α,4aα,7α,8aβ)]-4,4,7-Trimethyl-3-(2-methylallyl)-octahydrobenzo[*e*][1,3]oxazin-2-yl]-1-phenylbut-3-en-1-ol (7e): Colorless oil. $[\alpha]_D^{25}$ = –21.7 (*c* = 1.2, CH_2Cl_2). ^1H NMR: δ = 0.83–1.05 (m, 2 H), 0.91 (s, 3 H), 0.95 (d, *J* = 6.5 Hz, 3 H), 1.12 (m, 1 H), 1.15 (s, 3 H), 1.25 (s, 3 H), 1.44–1.63 (m, 3 H), 1.72 (m, 1 H), 1.95 (m, 1 H), 2.52 (dd, J_1 = 13.7, J_2 = 6.9 Hz, 1 H), 2.70 (dd, J_1 = 13.7, J_2 = 7.5 Hz, 1 H), 2.90 (d, *J* = 18.4 Hz, 1 H), 3.10 (s, 1 H), 3.60 (td, J_1 = 10.7, J_2 = 4.0 Hz, 1 H), 3.76 (d, *J* = 18.4 Hz, 1 H), 4.20 (s, 2 H), 4.90–4.97 (m, 2 H), 4.95 (s, 1 H), 5.54 (m, 1 H), 7.13 (m, 1 H),

7.23 (m, 2 H), 7.30 (m, 2 H) ppm. ^{13}C NMR: δ = 19.8, 22.2 (2 C), 24.9, 25.6, 31.4, 35.1, 41.4, 44.0, 48.3, 48.8, 57.9, 77.2, 77.5, 89.8, 108.5, 117.6, 125.9, 126.1 (2 C), 127.2 (2 C), 134.0, 142.3, 146.1 ppm. IR (film): $\tilde{\nu}$ = 3500 (broad), 3030, 1615, 1585, 745, 690, 680, 670, 620 cm^{-1}. $C_{25}H_{37}NO_2$ (383.57): C 78.28, H 9.72, N 3.65; found C 78.45, H 9.59, N 3.78.

(1*S*)-1-[[2*S*(2α,4aα,7α,8aβ)]-3-Allyl-4,4,7-trimethyl-octahydrobenzo-[*e*][1,3]oxazin-2-yl]-3-methyl-1-phenylbut-3-en-1-ol (7f): Colorless oil. $[\alpha]_D^{25}$ = –20.8 (*c* = 1.2, CH_2Cl_2). ^{1}H NMR: δ = 0.83–1.00 (m, 2 H), 0.93 (s, 3 H), 0.95 (d, *J* = 6.6 Hz, 3 H), 1.11 (m, 1 H), 1.22 (s, 3 H), 1.38 (s, 3 H), 1.42–1.63 (m, 3 H), 1.71 (m, 1 H), 1.95 (m, 1 H), 2.45 (d, *J* = 13.1 Hz, 1 H), 2.69 (d, *J* = 13.1 Hz, 1 H), 3.08 (dd, J_1 = 17.5, J_2 = 6.7 Hz, 1 H), 3.15 (s, 1 H), 3.60 (td, J_1 = 10.4, J_2 = 4.0 Hz, 1 H), 3.78 (m, 1 H), 4.47 (dd, J_1 = 10.1, J_2 = 1.2 Hz, 1 H), 4.52 (d, *J* = 1.2 Hz, 1 H), 4.54 (dd, J_1 = 17.6, J_2 = 1.2 Hz, 1 H), 4.72 (d, *J* = 1.2 Hz, 1 H), 4.84 (m, 1 H), 4.94 (s, 1 H), 7.16 (m, 1 H), 7.25 (m, 2 H), 7.35 (m, 2 H) ppm. ^{13}C NMR: δ = 22.2, 22.4, 24.2, 24.9, 26.8, 31.4, 35.1, 41.5, 44.7, 46.2, 52.8, 57.8, 77.3, 77.4, 89.5, 111.3, 114.7, 125.9, 126.4 (2 C), 126.9 (2 C), 142.2, 142.4, 142.5 ppm. IR (film): $\tilde{\nu}$ = 3505 (broad), 3040, 1620, 1585, 700, 680 cm^{-1}. $C_{25}H_{37}NO_2$ (383.57): C 78.28, H 9.72, N 3.65; found C 78.38, H 9.89, N 3.50.

(1*S*)-1-[[2*S*(2α,4aα,7α,8aβ)]-4,4,7-Trimethyl-3-(2-methylallyl)-octahydrobenzo[*e*][1,3]oxazin-2-yl]-1-phenylpent-4-en-1-ol (7g): Colorless oil. $[\alpha]_D^{25}$ = –26.3 (*c* = 0.9, CH_2Cl_2). ^{1}H NMR: δ = 0.83–1.00 (m, 2 H), 0.90 (s, 3 H), 0.95 (d, *J* = 6.5 Hz, 3 H), 1.11 (m, 1 H), 1.15 (s, 3 H), 1.24 (s, 3 H), 1.43–1.69 (m, 4 H), 1.63–1.78 (m, 2 H), 1.95 (m, 1 H), 2.02–2.14 (m, 2 H), 2.89 (d, *J* = 18.5 Hz, 1 H), 3.00 (s, 1 H), 3.62 (td, J_1 = 10.5, J_2 = 4.0 Hz, 1 H), 3.78 (d, *J* = 18.5 Hz, 1 H), 4.16 (s, 2 H), 4.81–4.91 (m, 2 H), 4.91 (s, 1 H), 5.71 (m, 1 H), 7.12 (m, 1 H), 7.22 (m, 2 H), 7.28 (m, 2 H) ppm. ^{13}C NMR: δ = 19.8, 22.3 (2 C), 24.9, 25.6, 27.4, 31.4, 35.1, 41.4, 43.3, 43.9, 48.3, 57.7, 77.4, 77.5, 90.6, 108.3, 113.8, 125.8, 126.1 (2 C), 127.3 (2 C), 139.2, 142.1, 146.0 ppm. IR (film): $\tilde{\nu}$ = 3500 (broad), 3060, 1630, 1590, 750, 725, 690 cm^{-1}. $C_{26}H_{39}NO_2$ (397.59): C 78.54, H 9.89, N 3.52; found C 78.40, H 10.00, N 3.43.

(3*S*)-3-[[2*S*(2α,4aα,7α,8aβ)]-3-Allyl-4,4,7-trimethyl-octahydrobenzo-[*e*][1,3]oxazin-2-yl]-2-methylhex-5-en-3-ol (7h): Colorless oil. $[\alpha]_D^{25}$ = –18.2 (*c* = 1.4, CH_2Cl_2). ^{1}H NMR: δ = 0.81–1.12 (m, 3 H), 0.92 (d, *J* = 6.5 Hz, 3 H), 0.94 (d, *J* = 6.9 Hz, 6 H), 1.06 (s, 3 H), 1.19 (s, 3 H), 1.40–1.58 (m, 3 H), 1.66 (m, 1 H), 1.82 (m, 1 H), 2.14 (sept, *J* = 6.9 Hz, 1 H), 2.27 (d, *J* = 7.1 Hz, 2 H), 2.64 (s, 1 H), 3.29 (dd, J_1 = 18.4, J_2 = 5.3 Hz, 1 H), 3.44 (td, J_1 = 10.6, J_2 = 4.0 Hz, 1 H), 4.12 (m, 1 H), 4.44 (s, 1 H), 4.89–5.04 (m, 3 H), 5.13 (dd, J_1 = 17.3, J_2 = 1.9 Hz, 1 H), 5.84–6.02 (m, 2 H) ppm. ^{13}C NMR: δ = 16.7, 17.8, 22.3, 22.5, 24.9, 26.9, 31.4, 32.1, 35.2, 40.4, 41.4, 43.9, 46.2, 58.3, 77.1, 77.3, 88.3, 112.6, 116.0, 135.7, 142.2 ppm. IR (film): $\tilde{\nu}$ = 3560 (broad), 3075, 1635, 680 cm^{-1}. $C_{21}H_{37}NO_2$ (335.52): C 75.17, H 11.12, N 4.17; found C 75.03, H 11.21, N 4.06.

(3*S*)-3-[[2*S*(2α,4aα,7α,8aβ)]-3-Allyl-4,4,7-trimethyl-octahydrobenzo-[*e*][1,3]oxazin-2-yl)-2-methylhept-6-en-3-ol (7i): Colorless oil. $[\alpha]_D^{25}$ = –28.4 (*c* = 0.9, CH_2Cl_2). ^{1}H NMR: δ = 0.82–1.03 (m, 2 H), 0.91 (d, *J* = 6.9 Hz, 3 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 0.93 (d, *J* = 6.4 Hz, 3 H), 1.05 (s, 3 H), 1.10 (m, 1 H), 1.20 (s, 3 H), 1.42–1.67 (m, 5 H), 1.72 (m, 1 H), 1.84 (m, 1 H), 2.05–2.18 (m, 3 H), 2.69 (s, 1 H), 3.29 (dd, J_1 = 18.4, J_2 = 5.3 Hz, 1 H), 3.47 (td, J_1 = 10.5, J_2 = 4.0 Hz, 1 H), 4.10 (m, 1 H), 4.42 (s, 1 H), 4.88–4.97 (m, 2 H), 5.02 (dd, J_1 = 17.1, J_2 = 1.8 Hz, 1 H), 5.13 (dd, J_1 = 17.3, J_2 = 1.8 Hz, 1 H), 5.75–5.98 (m, 2 H) ppm. ^{13}C NMR: δ = 16.6, 17.8, 22.2, 22.5, 24.9, 27.0, 28.6, 31.4, 32.2, 34.6, 35.2, 41.5, 43.8, 46.1, 58.2, 76.9, 77.4, 89.2, 112.7, 113.8, 140.0, 142.1 ppm. IR (film): $\tilde{\nu}$ = 3570 (broad), 3080, 1640 cm^{-1}. $C_{22}H_{39}NO_2$ (349.55): C 75.59, H 11.25, N 4.01; found C 75.74, H 11.12, N 4.14.

(1*R*)-1-[[2*S*(2α,4aα,7α,8aβ)]-3-Allyl-4,4,7-trimethyl-octahydrobenzo-[*e*][1,3]oxazin-2-yl]-1-phenylbut-3-en-1-ol (7j): Colorless oil. $[\alpha]_D^{25}$ = –1.9 (*c* = 0.8, $CHCl_3$). ^{1}H NMR: δ = 0.85–1.00 (m, 2 H), 0.92 (d, *J* = 6.6 Hz, 3 H), 1.05 (s, 3 H), 1.13 (m, 1 H), 1.27 (s, 3 H), 1.37–1.52 (m, 2 H), 1.56 (m, 1 H), 1.65 (m, 1 H), 1.92 (m, 1 H), 2.58–2.72 (m, 2 H), 2.99 (ddt, J_1 = 18.8, J_2 = 4.5, Hz, J_3 = 2.1 Hz, 1 H), 3.19 (ddt, J_1 = 18.8, J_2 = 4.5, J_3 = 2.0 Hz, 1 H), 3,43 (s, 1 H), 3.46 (td, J_1 = 10.6, J_2 = 3.9 Hz, 1 H), 4.88 (s, 1 H), 4.90–5.10 (m, 4 H), 5,52–5.71 (m, 2 H), 7.18–7.30 (m, 3 H), 7.56 (m, 2 H) ppm. ^{13}C NMR: δ = 22.2, 23.0, 24.9, 26.3, 31.4, 35.1, 41.1, 44.7, 45.1, 46.4, 53.4, 58.5, 75.6, 78.2, 90.8, 113.4, 117.7, 126.3 (2 C), 127.4 (2 C), 134.1, 141.0, 144.9 ppm. IR (film): $\tilde{\nu}$ = 3490, 3070, 1640, 760, 700 cm^{-1}. $C_{24}H_{35}NO_2$: C 78.00, H 9.55, N 3.79; found C 77.89, H 9.68, N 3.91.

RCM Reaction of Dienes 7a–j: A solution of bis(tricyclohexylphosphane)benzylideneruthenium dichloride (0.09 mmol, 74 mg) in CH_2Cl_2 (10 mL) was added to a solution of the corresponding **7a–i**·HCl[32] (3 mmol) in CH_2Cl_2 (290 mL). The resulting mixture was stirred at room temperature under argon for 15–30 h, and additional portions of catalyst were added after the times indicated in Table 2. Additional heating at reflux was necessary for ring-closing metathesis of compound **7f**. When the reaction was found to be complete, a saturated aqueous $NaHCO_3$ solution was added. The solution was extracted with CH_2Cl_2 (3×25 mL) and the combined extracts were dried over anhydrous $MgSO_4$ and concentrated under vacuum. The residue was purified by flash chromatography on silica gel with mixtures of hexanes/ethyl acetate as eluent.

(3*R*,4a*R*,5a*S*,6*S*,11a*S*)-3,11,11-Trimethyl-6-phenyl-2,3,4,4a,5a,6,7,10,11,11a-decahydro-1*H*-5-oxa-10a-azacyclohepta[*b*]naphthalen-6-ol (8a): Yellow oil. $[\alpha]_D^{25}$ = –123.6 (*c* = 0.9, CH_2Cl_2). ^{1}H NMR: δ = 0.81–0.94 (m, 2 H), 0.86 (d, *J* = 6.5 Hz, 3 H), 1.05 (m, 1 H), 1.15 (s, 3 H), 1.21 (s, 3 H), 1.24 (m, 1 H), 1.41–1.52 (m, 2 H), 1.63 (m, 1 H), 1.75 (m, 1 H), 2.26 (dd, J_1 = 14.8, J_2 = 8.0 Hz, 1 H), 3.08 (dd, J_1 = 13.8, J_2 = 8.3 Hz, 1 H), 3.17 (td, J_1 = 10.6, J_2 = 4.0 Hz, 1 H), 3.29 (m, 1 H), 3.62 (s, 1 H), 3.84 (dd, J_1 = 13.8, J_2 = 5.7 Hz, 1 H), 4.52 (s, 1 H), 5.73 (m, 1 H), 6.02 (m, 1 H), 7.19 (m, 1 H), 7.27 (m, 2 H), 7.62 (d, *J* = 8.7 Hz, 2 H) ppm. ^{13}C NMR: δ = 22.2 (2 C), 25.1, 28.7, 31.3, 34.4, 35.0, 38.0, 40.9, 45.8, 58.2, 71.6, 77.5, 92.0, 126.1 (2 C), 126.5, 127.3 (2 C), 130.3, 131.5, 146.5 ppm. IR (film): $\tilde{\nu}$ = 3500 (broad), 3030, 1600, 765, 720, 695, 640 cm^{-1}. $C_{22}H_{31}NO_2$ (341.49): C 77.38, H 9.15, N 4.10; found C 77.21, H 9.27, N 3.98.

(3*R*,4a*R*,5a*S*,6*S*,12a*S*)-6-Phenyl-3,12,12-trimethyl-2,3,4,4a,6,7,8,11,12,12a-decahydro-1*H*,5a*H*-5-oxa-11a-azacycloocta[*b*]naphthalen-6-ol (8b): Yellow oil $[\alpha]_D^{25}$ = –76.8 (*c* = 1.2, CH_2Cl_2). ^{1}H NMR (333 K): δ = 0.78–0.97 (m, 2 H), 0.88 (d, *J* = 6.5 Hz, 3 H), 1.04 (m, 1 H), 1.08 (s, 3 H), 1.21 (s, 3 H), 1.24–1.42 (m, 2 H), 1.55 (m, 1 H), 1.63 (m, 1 H), 1.86 (m, 1 H), 1.95 (m, 1 H), 2.26 (m, 1 H), 2.45 (m, 1 H), 2.80 (m, 1 H), 3.22 (m, 1 H), 3.24 (td, J_1 = 10.7, J_2 = 4.0 Hz, 1 H), 3.40 (s, 1 H), 3.85 (dd, J_1 = 15.5, J_2 = 8.8 Hz, 1 H), 4.52 (s, 1 H), 5.65 (m, 1 H), 5.78 (m, 1 H), 7.14 (m, 1 H), 7.23 (m, 2 H), 7.69 (d, *J* = 8.7 Hz, 2 H) ppm. ^{13}C NMR (333 K): δ = 21.4, 22.0, 24.8, 25.2, 27.7, 31.2, 35.0, 36.2, 38.0, 41.2, 47.6, 58.0, 75.2, 76.7, 90.0, 125.5 (2 C), 125.9, 127.2 (2 C), 128.1, 133.4, 150.1 ppm. IR (film): $\tilde{\nu}$ = 3490 (broad), 3060, 1600, 760, 735, 700 cm^{-1}. $C_{23}H_{33}NO_2$ (355.51): C 77.70, H 9.36, N 3.94; found C 77.59, H 9.23, N 3.82.

(3*R*,4a*R*,5a*S*,6*S*,11a*S*)-3,9,11,11-Tetramethyl-6-phenyl-2,3,4,4a,5a,6,7,10,11,11a-decahydro-1*H*-5-oxa-10a-azacyclohepta-[*b*]naphthalen-6-ol (8e): Colorless solid. M.p.: 122–123 °C (from

hexane). $[\alpha]_D^{25}$ = –106.5 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR: δ = 0.79–0.98 (m, 2 H), 0.86 (d, *J* = 6.5 Hz, 3 H), 1.06 (m, 1 H), 1.15 (s, 3 H), 1.23 (s, 3 H), 1.20–1.48 (m, 2 H), 1.52 (m, 1 H), 1.66 (m, 1 H), 1.74 (m, 1 H), 1.82 (t, *J* = 1.7 Hz, 3 H), 2.20 (dd, J_1 = 14.7, J_2 = 8.0 Hz, 1 H), 2.80 (d, *J* = 13.6 Hz, 1 H), 3.22 (m, 1 H), 3.19 (td, J_1 = 10.7, J_2 = 4.0 Hz, 1 H), 3.47 (s, 1 H), 3.93 (d, *J* = 13.6 Hz, 1 H), 4.48 (s, 1 H), 5.38 (m, 1 H), 7.18–7.33 (m, 3 H), 7.61 (d, *J* = 8.6 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.7, 22.1, 23.3, 25.1, 28.7, 31.2, 34.1, 34.9, 40.8, 43.0, 46.1, 57.8, 71.7, 77.0, 92.0, 122.6, 126.0 (2 C), 126.3, 127.1 (2 C), 140.7, 146.3 ppm. IR (nujol dispersion): $\tilde{\nu}$ = 3490 (broad), 3040, 1590, 760, 750, 690 cm^{-1}. $C_{23}H_{33}NO_2$ (355.51): C 77.70, H 9.36, N 3.94; found C 77.83, H 9.51, N 4.03.

(3*R*,4a*R*,5a*S*,6*S*,11a*S*)-3,8,11,11-Tetramethyl-6-phenyl-2,3,4,4a,5a,7,7,10,11,11a-decahydro-1*H*-5-oxa-10a-azacyclohepta-[*b*]naphthalen-6-ol (8f): Yellow oil. $[\alpha]_D^{25}$ = –78.5 (*c* = 0.8, CH_2Cl_2). ^{1}H NMR: δ = 0.78–0.94 (m, 2 H), 0.86 (d, *J* = 6.5 Hz, 3 H), 1.04 (m, 1 H), 1.15 (s, 3 H), 1.21 (s, 3 H), 1.31 (m, 1 H), 1.45 (m, 1 H), 1.52 (m, 1 H), 1.59–1.73 (m, 2 H), 1.69 (s, 3 H), 2.12 (d, *J* = 14.2 Hz, 1H), 2.97 (dd, J_1 = 13.8, J_2 = 8.4 Hz, 1 H), 3.18 (td, J_1 = 10.6, J_2 = 3.9 Hz, 1 H), 3.44 (d, *J* = 14.2, 1 H), 3.57 (s, 1 H), 3.78 (dd, J_1 = 13.8, J_2 = 6.1 Hz, 1 H), 4.49 (s, 1 H), 5.71 (m, 1 H), 7.18–7.35 (m, 3 H), 7.63 (d, *J* = 8.6 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.7, 22.1, 25.0, 26.2, 28.5, 31.2, 34.9, 37.8, 39.6, 40.7, 45.8, 57.9, 71.3, 77.0, 92.1, 124.0, 126.2 (2 C), 126.4, 127.2 (2C), 139.6, 146.5 ppm. IR (film): $\tilde{\nu}$ = 3600, 3040, 1600, 700, 735, 670 cm^{-1}. $C_{23}H_{33}NO_2$ (355.51): C 77.70, H 9.36, N 3.94; found C 77.86, H 9.25, N 4.07.

(3*R*,4a*R*,5a*S*,6*S*,11a*S*)-6-Isopropyl-3,11,11-trimethyl-2,3,4,4a,5a,6,7,10,11,11a-decahydro-1*H*-5-oxa-10a-azacyclohepta-[*b*]naphthalen-6-ol (8h): Yellow oil. $[\alpha]_D^{25}$ = –88.1 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR: δ = 0.84–1.06 (m, 2 H), 0.92 (d, *J* = 6.5 Hz, 3 H), 0.98 (d, *J* = 6.8 Hz, 3 H), 0.99 (d, *J* = 6.8 Hz, 3 H), 1.11 (m, 1 H), 1.19 (s, 6 H), 1.34–1.52 (m, 2 H), 1.56 (m, 1 H), 1.70 (m, 1 H), 1.80 (sept, *J* = 6.8 Hz, 1 H), 1.89 (m, 1 H), 2.11 (dd, J_1 = 15.0, J_2 = 8.2 Hz, 1 H), 2.63 (dt, J_1 = 15.0, J_2 = 3.3 Hz, 1 H), 2.84 (s, 1 H), 3.01 (dd, J_1 = 13.9, J_2 = 7.8 Hz, 1 H), 3.43 (td, J_1 = 10.6, J_2 = 4.0 Hz, 1 H), 3.68 (dd, J_1 = 13.9, J_2 = 5.7, 1 H), 4.62 (s, 1 H), 5.68 (m, 1 H), 5.96 (m, 1 H) ppm. ^{13}C NMR: δ = 17.3 (2 C), 21.8, 22.1, 25.1, 28.5, 30.8, 31.3, 34.9, 36.5, 37.7, 41.1, 46.1, 58.1, 71.3, 77.1, 89.9, 130.3, 131.7 ppm. IR (film): $\tilde{\nu}$ = 3525, 3040, 700 cm^{-1}. $C_{19}H_{33}NO_2$ (307.47): C 74.22, H 10.82, N 4.56; found C 74.38, H 10.87, N 4.43.

(3*R*,4a*R*,5a*S*,6*S*,12a*S*)-6-Isopropyl-3,12,12-trimethyl-2,3,4,4a,6,7,8,11,12,12a-decahydro-1*H*,5a*H*-5-oxa-11a-azacyclo-octa[*b*]naphthalen-6-ol (8i): Colorless solid, M.p.. 83–84 °C (from hexane). $[\alpha]_D^{25}$ = –50.2 (*c* = 1.2, CH_2Cl_2). ^{1}H NMR (333 K): δ = 0.85–1.14 (m, 3 H), 0.93 (d, *J* = 6.5 Hz, 3 H), 0.95 (d, *J* = 6.8 Hz, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 1.19 (s, 3 H), 1.20 (s, 3 H), 1.31 (m, 1 H), 1.48 (m, 1 H), 1.56–1.76 (m, 3 H), 1.78–1.96 (m, 2 H), 2.21–2.49 (m, 3 H), 2.80 (s, 1 H), 3.00 (m, 1 H), 3.45 (td, J_1 = 10.6, J_2 = 3.9 Hz, 1 H), 3.76 (m, 1 H), 4.55 (s, 1 H), 5.55 (m, 1 H), 5.72 (m, 1 H) ppm. ^{13}C NMR (333 K): δ = 17.3, 17.5, 21.7, 22.1, 25.3, 25.5, 27.9, 29.4, 31.5, 35.2, 37.8, 39.2, 41.5, 47.3, 58.3, 74.8, 76.7, 87.9, 127.8, 133.4 ppm. IR (nujol dispersion): $\tilde{\nu}$ = 3495, 3040 cm^{-1}. $C_{20}H_{35}NO_2$ (321.50): C 74.72, H 10.97, N 4.36; found C 74.59, H 11.11, N 4.23.

(3*R*,4a*R*,5a*S*,6*R*,11a*S*)-3,11,11-Trimethyl-6-phenyl-2,3,4,4a,5a,6,7,10,11,11a-decahydro-1*H*-5-oxa-10a-azacyclohepta-[*b*]naphthalen-6-ol (8j): Yellow oil. $[\alpha]_D^{25}$ = –24.8 (*c* = 0.7, CH_2Cl_2). ^{1}H NMR: δ = 0.81–0.92 (m, 2 H), 0.86 (d, *J* = 6.5 Hz, 3 H), 1.01 (m, 1 H), 1.22 (s, 3 H), 1.28 (s, 3 H), 1.27–1.37 (m, 2 H), 1.56 (m, 1 H), 1.65 (m, 1 H), 1.73 (m, 1 H), 2.32 (dd, J_1 = 16.4, J_2 = 7.1 Hz, 1 H), 2.99 (m, 1 H), 3.24 (dd, J_1 = 16.4, J_2 = 7.1 Hz, 1 H), 3.39 (td, J_1 = 10.6, J_2 = 4.0 Hz, 1 H), 3.66 (s, 1 H), 3.73 (m, 1 H), 5.04 (s, 1 H), 5,54 (m, 1 H), 5,82 (m, 1 H), 7.23 (m, 1 H), 7.33 (m, 2 H), 7.51 (m, 2 H) ppm. ^{13}C NMR: δ = 21.2, 22.1, 25.0, 28.1, 31.1, 34.9, 38.7, 40.4, 40.9, 46.1, 57.8, 76.1, 77.1, 89.9, 124.6 (2 C), 126.0, 126.4, 127.9 (2 C), 130.6, 149.1 ppm. IR (film): $\tilde{\nu}$ = 3530, 3020, 1450, 760, 730, 700 cm^{-1}. $C_{22}H_{31}NO_2$: C 77.38, H 9.15, N 4.10; found C 78.51, H 9.29, N 3.98.

Synthesis of Amino Alcohols 9a, 9b, 9e, 9f, 9h, and 9i. General Method: Dry $AlCl_3$ (0.48 g, 3.6 mmol) was added in portions to a suspension of $LiAlH_4$ (0.41 g, 10.8 mmol) in THF (30 mL) cooled to –10 °C. The mixture was stirred for an additional 10 min, and a solution of the corresponding benzoxazine **8a**–**i** (2.16 mmol) in THF (20 mL) was slowly added. The mixture was stirred for 15 min at room temperature and was then heated at reflux for 10 min. It was then allowed to reach room temperature and quenched by addition of 10% aqueous NaOH (2 mL). The mixture was filtered, the solid was washed with hot ethyl acetate, and the organic layer was dried over $MgSO_4$. The solvent was eliminated under vacuum, and the residue was chromatographed on silica gel with hexanes/ethyl acetate 8:1 as eluent.

(3*S*)-*N*-(8-Mentholyl)-3-phenyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (9a): 719.7 mg, 97% from **8a**. Colorless solid. M.p.. 128–129 °C (from hexane). $[\alpha]_D^{25}$ = +169.2 (*c* = 0.9, CH_2Cl_2). ^{1}H NMR (333 K): δ = 0.83–1.04 (m, 2 H), 0.87 (s, 3 H,), 0.94 (d, *J* = 6.5 Hz, 3 H), 1.12 (m, 1 H), 1.20 (s, 3 H), 1.44 (m, 1 H), 1.53–1.73 (m, 2 H), 1.86–2.05 (m, 2 H), 2.47 (dd, J_1 = 15.0, J_2 = 8.4 Hz, 1 H), 2.78 (m, 1 H), 2.81 (d, *J* = 14.8 Hz, 1 H), 3.19 (d, *J* = 14.8 Hz, 1 H), 3.21 (m, 1 H), 3.62–3.76 (m, 2 H), 5.09 (s, broad, 1 H), 5.48 (m, 1 H), 5.70 (m, 1 H), 7.19 (m, 1 H), 7.27 (m, 2 H), 7.59 (d, *J* = 8.7 Hz, 2 H), 8.45 (s, broad, 1 H) ppm. ^{13}C NMR (333 K): δ = 16.6, 21.0, 21.8, 25.8, 31.1, 34.9, 39.3, 43.8, 47.9, 51.2, 61.6, 62.2, 73.5, 77.8, 124.9 (2 C), 125.0, 126.7, 127.9 (2 C), 128.0, 146.8 ppm. IR (nujol dispersion): $\tilde{\nu}$ = 3360 (broad), 1600, 790, 770, 705, 670 cm^{-1}. $C_{22}H_{33}NO_2$ (343.50): C 76.92, H 9.68, N 4.08; found C 77.07, H 9.82, N 4.21.

(3*S*)-*N*-(8-Mentholyl)-3-phenyl-1,2,3,4,5,8-hexahydroazocin-3-ol (9b): 756.8 mg, 98% from **8b**. Colorless oil. $[\alpha]_D^{25}$ = +76.1 (*c* = 1.2, CH_2Cl_2). ^{1}H NMR (333 K): δ = 0.78–1.02 (m, 2 H), 0.87 (s, 3 H), 0.92 (d, *J* = 6.5 Hz, 3 H), 1.09 (m, 1 H), 1.20 (s, 3 H), 1.42 (m, 1 H), 1.53 (m, 1 H), 1.64 (m, 1 H), 1.78 (m, 1 H), 1.89–2.06 (m, 2 H), 2.12–2.40 (m, 2 H), 2.62 (m, 1 H), 2.78 (d, *J* = 14.4 Hz, 1 H), 3.11 (d, *J* = 14.4 Hz, 1 H), 3.21 (m, 1 H), 3.58–3.72 (m, 2 H), 5.30 (s, broad, 1 H), 5.66 (m, 1 H), 5.82 (m, 1 H), 7.26 (m, 1 H), 7.38 (m, 2 H), 7.59 (m, 2 H), 8.55 (s, broad, 1 H) ppm. ^{13}C NMR (333 K): δ = 19.4, 21.6, 21.8, 23.5, 26.1, 31.1, 35.0, 38.7, 43.5, 47.5, 47.8, 61.7, 62.0, 73.3, 74.7, 124.7 (2 C), 126.4, 126.8, 127.9 (2 C), 133.5, 149.0 ppm. IR (film): $\tilde{\nu}$ = 3390 (broad), 3060, 1601, 760, 735, 700 cm^{-1}. $C_{23}H_{35}NO_2$ (357.53): C 77.27, H 9.87, N 3.92; found C 77.38, H 9.71, N 4.05.

(3*S*)-*N*-(8-Mentholyl)-6-methyl-3-phenyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (9e): 758.8 mg, 98% from **8e**. Colorless solid. M.p.: 165–166 °C (from hexane). $[\alpha]_D^{25}$ = +143.8 (*c* = 0.9, CH_2Cl_2). ^{1}H NMR (333 K): δ = 0.88 (s, 3 H), 0.79–1.05 (m, 2 H), 0.93 (d, *J* = 6.5 Hz, 3 H), 1.13 (m, 1 H), 1.23 (s, 3 H), 1.44 (m, 1 H), 1.55–1.72 (m, 2 H), 1.68 (s, 3 H), 1.82–2.02 (m, 2 H), 2.41 (dd, J_1 = 14.9, J_2 = 8.5 Hz, 1 H), 2.72 (m, 1 H), 2.73 (d, *J* = 14.6 Hz, 1 H), 3.06 (d, *J* = 16.0 Hz, 1 H), 3.20 (d, *J* = 14.6 Hz, 1 H), 3.63 (d, *J* = 16.0 Hz, 1 H), 3.72 (td, J_1 = 10.3, J_2 = 3.9 Hz, 1 H), 4.96 (s, broad, 1 H), 5.49 (m, 1 H), 7.21 (m, 1 H), 7.29 (m, 2 H), 7.57 (m, 2 H), 8.42 (s, broad, 1 H) ppm. ^{13}C NMR (333 K): δ = 16.4, 20.9, 21.8, 23.3, 25.6, 30.9, 34.6, 38.5, 43.5, 47.4, 55.1, 61.5, 61.9, 73.3, 77.9, 120.0, 124.8 (2 C), 126.7, 127.8 (2 C), 134.4, 146.4 ppm. IR (nujol disper-

sion): $\tilde{\nu}$ = 3370 (broad), 1600, 755, 700 cm^{-1}. $C_{23}H_{35}NO_2$ (357.53): C 77.27, H 9.87, N 3.92; found C 77.43, H 9.75, N 4.08.

(3*S*)-*N*-(8-Mentholyl)-5-methyl-3-phenyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (9f): 679.6 mg, 88% from **8f**. Colorless oil. $[\alpha]_D^{25}$ = +69.0 (*c* = 1.0, CH_2Cl_2). ^1H NMR (333 K): δ = 0.81–1.02 (m, 2 H), 0.88 (s, 3 H), 0.93 (d, *J* = 6.6 Hz, 3 H), 1.11 (m, 1 H), 1.20 (s, 3 H), 1.31–1.72 (m, 3 H), 1.65 (s, 3 H), 1.86 (m, 1 H), 2.01 (m, 1 H), 2.23 (d, *J* = 14.5 Hz, 1 H), 2.89 (d, *J* = 14.6 Hz, 1 H), 2.98 (d, *J* = 14.5 Hz, 1 H), 3.19 (d, *J* = 14.5 Hz, 1 H), 3.21 (m, 1 H), 3.60–3.71 (m, 2 H), 5.02 (s, broad, 1 H), 5.31 (m, 1 H), 7.15–7.33 (m, 3 H), 7.57–7.60 (m, 2 H), 9.20 (s, 1 H) ppm. ^{13}C NMR (333 K): δ = 16.3, 21.0, 21.9, 25.9, 27.1, 31.2, 34.9, 44.0, 45.3, 47.8, 50.5, 61.7, 61.8, 73.5, 76.6, 121.8, 124.9 (2 C), 126.7, 127.9 (2 C), 133.0, 146.9 ppm. IR (nujol dispersion): $\tilde{\nu}$ = 3390, 700, 720, 750 cm^{-1}. $C_{23}H_{35}NO_2$ (357.53): C 77.27, H 9.87, N 3.92; found C 77.40, H 10.03, N 3.79.

(3*S*)-*N*-(8-Mentholyl)-3-isopropyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (9h): 615.0 mg, 92% from **8h**. Colorless oil. $[\alpha]_D^{25}$ = +54.6 (*c* = 1.1, CH_2Cl_2). ^1H NMR (333 K): δ = 0.87–1.14 (m, 3 H), 0.90 (d, *J* = 6.4 Hz, 3 H), 0.91 (s, 3 H), 0.95 (d, *J* = 6.9 Hz, 6 H), 1.19 (s, 3 H), 1.41 (m, 1 H), 1.60–1.77 (m, 3 H), 1.83 (m, 1 H), 1.94 (m, 1 H), 2.22 (dd, J_1 = 15.0, J_2 = 8.4 Hz, 1 H), 2.41 (m, 1 H), 2.60 (d, *J* = 14.3 Hz, 1 H), 3.00 (d, *J* = 14.3 Hz, 1 H), 3.14 (m, 1 H), 3.58–3.71 (m, 2 H), 4.50 (s, broad, 1 H), 5.34 (m, 1 H), 5.51 (m, 1 H), 8.40 (s, broad, 1 H) ppm. ^{13}C NMR (333 K): δ = 16.6, 16.9, 17.7, 21.1, 21.8, 26.0, 31.2, 35.0, 35.1, 35.9, 44.0, 47.9, 51.1, 58.1, 61.8, 73.4, 78.1, 125.2, 127.1 ppm. IR (film): $\tilde{\nu}$ = 3415, 1615, 800, 670 cm^{-1}. $C_{19}H_{35}NO_2$ (309.49): C 73.74, H 11.40, N 4.53; found C 73.91, H 11.28, N 4.68.

(3*S*)-*N*-(8-Mentholyl)-3-isopropyl-1,2,3,4,5,8-hexahydroazocin-3-ol (9i): 614.9 mg, 88% from **8i**. Colorless oil. $[\alpha]_D^{25}$ = +18.7 (*c* = 1.3, CH_2Cl_2). ^1H NMR (333 K): δ = 0.78–1.22 (m, 3 H), 0.83 (d, *J* = 6.5 Hz, 3 H), 0.87 (s, 3 H), 0.88 (d, *J* = 6.5 Hz, 3 H), 0.90 (d, *J* = 6.5 Hz, 3 H), 1.15 (s, 3 H), 1.36 (m, 1 H), 1.50–1.80 (m, 6 H), 1.88 (m, 1 H), 2.04 (m, 1 H), 2.41 (m, 1 H), 2.55 (d, *J* = 13.7 Hz, 1 H), 2.88 (d, *J* = 13.7 Hz, 1 H), 3.17 (m, 1 H), 3.51–3.62 (m, 2 H), 5.21 (s, broad, 2 H), 5.42 (m, 1 H), 5.74 (m, 1 H) ppm. ^{13}C NMR (333 K): δ = 17.0, 17.2, 21.1, 21.7, 21.9, 23.6, 26.3, 31.2, 34.6, 35.3, 38.2, 44.1, 45.2, 48.0, 53.9, 62.3, 73.1, 74.5, 125.8, 134.4 ppm. IR (film): $\tilde{\nu}$ = 3400, 1600, 730 cm^{-1}. $C_{20}H_{37}NO_2$ (323.51): C 74.25, H 11.53, N 4.33; found C 74.11, H 11.46, N 4.49.

(3R)-*N*-(8-Mentholyl)-3-phenyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (9j): Yield: 97%. Colorless solid. M.p.: 135–136 °C (from hexane). $[\alpha]_D^{25}$ = –68.8 (*c* = 0.7, CH_2Cl_2). ^1H NMR (333 K): δ = 0.82–1.09 (m, 3 H), 0.91 (s, 3 H), 0.91 (d, *J* = 6.5 Hz, 3 H), 1.24 (s, 3 H), 1.38–1.69 (m, 5 H), 1.93 (m, 1 H), 2.61 (m, 1 H), 2.77 (m, 1 H), 2.80 (d, *J* = 13.7 Hz, 1 H), 3.04 (m, 1 H), 3.23 (dd, J_1 = 13.7, J_2 = 2.2 Hz, 1 H), 3.68 (td, J_1 = 10.3, J_2 = 3.9 Hz, 1 H), 3.83 (m, 1 H), 4.92 (s, broad, 1 H), 5.70–5.89 (m, 2 H), 7.24 (m, 1 H), 7.33 (m, 2 H), 7.53 (m, 2 H) ppm. ^{13}C NMR (333 K): δ = 19.3, 21.9, 22.1, 26.4, 31.0, 35.2, 39.9, 44.6, 47.8, 50.6, 61.7, 62.6, 72.6, 75.9, 124.6, 126.9, 126.9, 128.1 (3C), 130.4, 147.5 ppm. IR (Nujol): $\tilde{\nu}$ = 3280 (broad), 760, 725, 700 cm^{-1}. $C_{22}H_{35}NO_2$: C 76.92, H 9.68, N 4.08; found C 77.16, H 9.54, N 3.96.

Removal of the Menthol Appendage. General Method: A solution of the corresponding aminomenthol derivative **9a**, **9b**, **9e**, **9f**, **9h**, or **9i** (1.48 mmol) and PCC (1.28 g, 5.95 mmol) in CH_2Cl_2 (35 mL) was stirred at room temperature with 3-Å molecular sieves (2.5 g) until the oxidation was complete (TLC, 40–70 h). The solvent was eliminated under reduced pressure, the residue was dissolved in a 10% aqueous solution of NaOH (40 mL), and the resulting solution was extracted with $CHCl_3$ (5×25 mL). The organic layer was washed with brine and dried over $MgSO_4$, and the solvents were evaporated under vacuum. The residue was redissolved in a MeOH/THF mixture (1:2, 12 mL) and an aqueous solution of KOH (2.5 M, 4 mL) was then added. The mixture was stirred at room temperature for 2–3 days. After removal of the solvents under vacuum, H_2O (30 mL) was added and the mixture was extracted with $CHCl_3$ (4×25 mL). The organic layer was washed with H_2O and dried over $MgSO_4$, and the solvent was eliminated under vacuum. The residue was chromatographed on silica gel with a $CHCl_3$/EtOH mixture (8:1) as eluent.

(3*S*)-3-Phenyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (10a): 137.2 mg, 49% from **9a**. Colorless oil. $[\alpha]_D^{25}$ = –61.2 (*c* = 0.9, CH_2Cl_2). ^1H NMR: δ = 2.52 (ddd, J_1 = 16.2, J_2 = 7.7, J_3 = 1.5 Hz, 1 H), 2.75 (dq, J_1 = 16.2, J_2 = 2.7 Hz, 1 H), 3.04 (dd, *J* = 13.1, J_2 = 1.5 Hz, 1 H), 3.11 (d, *J* = 13.1 Hz, 1 H), 3.37 (dq, J_1 = 15.9, J_2 = 2.7 Hz, 1 H), 3.53 (dd, J_1 = 15.9, J_2 = 7.0 Hz, 1 H), 3.65 (s, broad, 2 H), 5.69 (m, 1 H), 5.91 (m, 1 H), 7.26 (m, 1 H), 7.34 (m, 2 H), 7.49 (m, 2 H) ppm. ^{13}C NMR: δ = 42.9, 48.6, 62.3, 71.7, 124.1 (2 C), 126.7, 127.3, 128.1 (2 C), 130.7, 147.1 ppm. IR (film): $\tilde{\nu}$ = 3330, 3025, 1600, 760, 700 cm^{-1}. $C_{12}H_{15}NO$ (189.25): C 76.16, H 7.99, N 7.40; found C 76.01, H 8.17, N 7.36.

(3R)-3-Phenyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (*ent*-10a): Yield: 50%. Colorless oil. $[\alpha]_D^{25}$ = +60.0 (*c* = 0.9, CH_2Cl_2). ^1H NMR, ^{13}C NMR, and IR data are coincident with those reported for **10a**.

(3*S*)-3-Phenyl-1,2,3,4,5,8-hexahydroazocin-3-ol (10b): 175.5 mg, 58% from **9b**. Colorless oil. $[\alpha]_D^{25}$ = +79.2 (*c* = 1.1, CH_2Cl_2). ^1H NMR (333 K): δ = 1.78–1.91 (m, 2 H), 2.01 (m, 1 H), 2.80 (s, broad, 2 H), 2.86 (dd, J_1 = 13.7, J_2 = 1.5 Hz, 1 H), 2.88 (m, 1 H), 3.21 (d, *J* = 13.7 Hz, 1 H), 3.52 (ddt, J_1 = 16.2, J_2 = 5.6, J_3 = 1.5 Hz, 1 H), 3.69 (dt, J_1 = 16.2, J_2 = 2.8 Hz, 1 H), 5.42 (m, 1 H), 5.91 (m, 1 H), 7.22 (m, 1 H), 7.31 (m, 2 H), 7.43 (m, 2 H) ppm. ^{13}C NMR (333 K): δ = 21.4, 42.5, 47.8, 55.4, 72.2, 124.1 (2 C), 126.1, 126.3, 128.1 (2 C), 132.5, 148.2 ppm. IR (film): $\tilde{\nu}$ = 3500, 3025, 1600, 760, 705 cm^{-1}. $C_{13}H_{17}NO$ (203.28): C 76.81, H 8.43, N 6.89; found C 76.94, H 8.57, N 6.77.

(3*S*)-6-Methyl-3-phenyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (10e): 162.5 mg, 54% from **9e**. Colorless oil. $[\alpha]_D^{25}$ = –95.7 (*c* = 0.9, CH_2Cl_2). ^1H NMR: δ = 1.78 (s, 3 H), 2.41 (ddd, J_1 = 15.8, J_2 = 8.2, J_3 = 1.5 Hz, 1 H), 2.76 (dq, J_1 = 15.8, J_2 = 1.5 Hz, 1 H), 3.01 (dd, J_1 = 13.0, J_2 = 1.5 Hz, 1 H), 3.06 (s, broad, 2 H), 3.09 (d, *J* = 13.0 Hz, 1 H), 3.31 (d, *J* = 15.4 Hz, 1 H), 3.41 (dt, J_1 = 15.4, J_2 = 1.5 Hz, 1 H), 5.38 (m, 1 H), 7.21 (m, 1 H), 7.30 (m, 2 H), 7.47 (m, 2 H). NMR: δ = 24.6, 41.6, 53.5, 63.2, 71.8, 120.8, 124.1 (2 C), 126.6, 128.1 (2 C), 140.5, 147.1 ppm. IR (film): $\tilde{\nu}$ = 3500, 3065, 3025, 1600, 765, 700 cm^{-1}. $C_{13}H_{17}NO$ (203.28): C 76.81, H 8.43, N 6.89; found C 76.69, H 8.52, N 6.72.

(3*S*)-5-Methyl-3-phenyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (10f): 135.4 mg, 45% from **9e**. Colorless oil. $[\alpha]_D^{25}$ = –98.6 (*c* = 1.0, CH_2Cl_2). ^1H NMR: δ = 1.77 (s, 3 H), 2.31 (d, *J* = 15.3 Hz, 1 H), 2.96 (d, *J* = 15.3 Hz, 1 H), 3.05 (d, *J* = 12.7 Hz, 1 H), 3.07 (s, broad, 2 H), 3.08 (d, *J* = 12.7 Hz, 1 H), 3.26 (m, 1 H), 3.39 (dd, J_1 = 15.2, J_2 = 7.3 Hz, 1 H), 5.73 (m, 1 H), 7.21 (m, 1 H), 7.36 (m, 2 H), 7.48 (m, 2 H) ppm. ^{13}C NMR: δ = 27.6, 47.2, 47.5, 63.5, 70.7, 124.0 (2C), 124.7, 126.6, 128.0 (2C), 136.9, 147.2 ppm. IR (film): $\tilde{\nu}$ = 3340,3060, 3030, 1600, 760, 700 cm^{-1}. $C_{13}H_{17}NO$ (203.28): C 76.81, H 8.43, N 6.89; found C 76.95, H 8.56, N 6.98.

(3*S*)-3-Isopropyl-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (10h): 117.2 mg, 51% from **9h**. Colorless oil. $[\alpha]_D^{25}$ = –42.1 (*c* = 1.1, CH_2Cl_2). ^1H NMR: δ = 0.92 (d, *J* = 6.9 Hz, 3 H), 0.98 (d, *J* = 6.9 Hz, 3 H), 1.79 (sept, *J* = 6.9 Hz, 1 H), 2.30 (dq, J_1 = 15.4, J_2 = 1.6 Hz, 1 H), 2.36 (dd, J_1 = 15.4, J_2 = 6.7 Hz, 1 H), 2.88 (d, *J* = 13.0 Hz, 1 H), 3.04 (d, *J* = 13.0 Hz, 1 H), 3.34 (dq, J_1 = 16.1, J_2 = 1.6 Hz, 1 H),

3.58 (dd, J_1 = 16.1, J_2 = 6.0 Hz, 1 H), 4.68 (s, broad, 2 H), 5.69 (m, 1 H), 5.75 (m, 1 H) ppm. ^{13}C NMR: δ = 16.9 (2 C), 35.9, 37.3, 48.1, 57.8, 72.1, 128.0, 128.3 ppm. IR (film): $\tilde{\nu}$ = 3325, 3010, 1700, 730, 660 cm^{-1}. $C_9H_{17}NO$ (155.24): C 69.63, H 11.04, N 9.02; found C 69.48, H 10.89, N 9.21.

(3*S*)-3-Isopropyl-1,2,3,4,5,8-hexahydroazocin-3-ol (10i): (125.2 mg, 50% from **9i**). Colorless oil. $[\alpha]_D^{25}$ = +44.0 (c = 0.6, CH_2Cl_2). ^{1}H NMR (333 K): δ = 0.85 (d, J = 6.9 Hz, 3 H), 0.93 (d, J = 6.9 Hz, 3 H), 1.47 (m, 1 H), 1.60–1.69 (m, 2 H), 1.97 (m, 1 H), 2.68 (m, 1 H), 2.72 (dd, J_1 = 13.6, J_2 = 1.6 Hz, 1 H), 2.83 (d, J = 13.6 Hz, 1 H), 3.08 (s, broad, 2 H), 3.45 (dd, J_1 = 16.1, J_2 = 5.8 Hz, 1 H), 3.62 (dt, J_1 = 16.1, J_2 = 1.6 Hz, 1 H), 5.37 (m, 1 H), 5.87 (m, 1 H) ppm. ^{13}C NMR: δ = 16.7, 17.1, 20.9, 34.0, 38.3, 47.0, 52.1, 71.9, 125.7, 133.3 ppm. IR (film): $\tilde{\nu}$ = 3350, 3010, 1700, 730, 710 cm^{-1}. $C_{10}H_{19}NO$ (169.26): C 70.96, H 11.31, N 8.28; found C 70.76, H 11.49, N 8.01.

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