

Synthesis of Enantiopure Oxygen- and Nitrogen-Containing Heterocycles by Diastereoselective Ring-Closing Metathesis Reaction in Perhydro-1,3-benzoxazine Derivatives

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Abstract. Diastereoselective ring-closing metathesis reactions on chiral trienic perhydro-1,3-benzoxazines derived from (-)-8-aminomenthol featuring two diastereotopic olefin chains is described. The diastereochemical outcome of the cyclization appeared to be dependent on the length and position of the olefin chains in perhydro-1,3-benzoxazine, the degree of substitution of the double bonds and the ruthenium catalyst used. After separation of the diastereomers, and removal of the chiral auxiliary, enantiopure oxygen- and nitrogen-containing heterocycles were obtained.

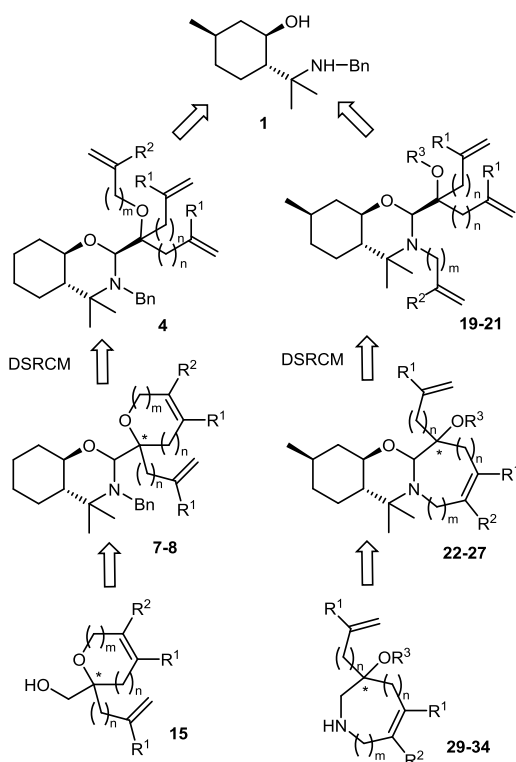
Keywords: Asymmetric synthesis; metathesis; oxygen heterocycles; nitrogen heterocycles; chiral auxiliaries

1 Introduction

Partially unsaturated oxygen and nitrogen-containing heterocycles are common subunits displayed in a broad array of interesting and useful biologically active molecules as well as natural products.^[1] Among a large number of synthetic approaches, the ring-closing metathesis (RCM) reaction has emerged as one of the most efficient ways to prepare different-sized heterocycles.^[2-4] A wide range of enantioenriched heterocycles can be accessed by asymmetric ring-closing metathesis (ARCM), asymmetric ring-opening/cross-metathesis (AROXM) or asymmetric ring rearrangements (ARR) starting from racemic or pro-chiral compounds in the presence of chiral well-defined molybdenum- and ruthenium-based metathesis catalysts.^[5] Despite progress in chiral catalyst design, however, a significant challenge remains, ARCM of unhindered trienes has so far been unsuccessful, resulting in extremely low enantioselectivities.^[6] In these cases, the diastereoselective ring-closing metathesis reaction (DSRCM)^[7] in substrates in which an existing chiral centre controls the direction of cyclization could compete advantageously over an enantioselective RCM reaction using chiral alkylidene complexes. Under certain reaction conditions the DSRCM

cyclization may be reversible and the observed diastereomer ratios reflect a thermodynamic preference.^[8] If one of the diastereomers is energetically much more favoured good diastereoselectivities can be achieved not only under kinetic control, but also under thermodynamic control.^[9] On the other hand, the diastereomers could be easily separated by chromatography and the desired product can be obtained optically pure.^[10]

Over the last few years, we have shown that chiral perhydro-1,3-benzoxazines derived from (-)-8-aminomenthol constitute useful chiral auxiliaries in different diastereoselective cycloaddition and cyclization processes.^[11] We now report on the synthesis of enantiopure cyclic ethers and amines by DSRCM reaction on trienic perhydro-1,3-benzoxazines with two diastereotopic olefinic groups derived from (-)-8-aminomenthol acting as chiral template.^[12] Scheme 1 summarizes our intentions. In general, performing DSRCM metathesis reactions with high diastereoselectivity requires that the olefins at the prochiral centre do not react with each other and also that the primary attack of the catalyst occurs at the double bond of the other olefin.^[7a]



Scheme 1. Retrosynthetic approach to chiral oxygen and nitrogen-containing heterocycles.

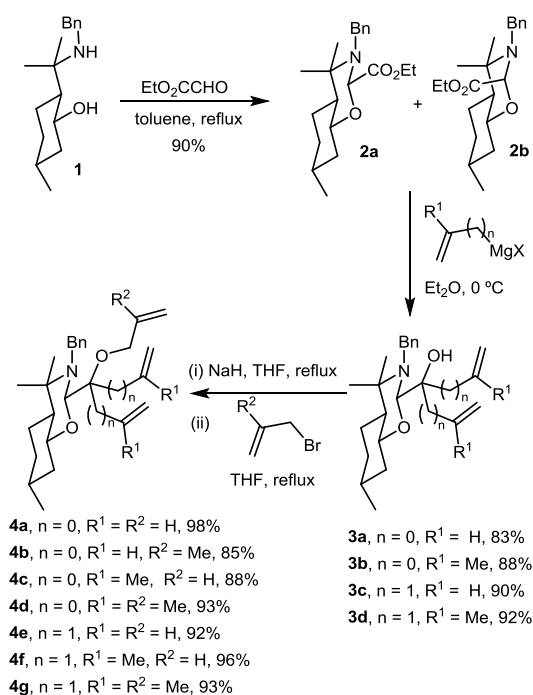
Results and Discussion

Synthesis of chiral cyclic ethers

The starting trienic perhydro-1,3-benzoxazines **4a-j** were prepared as single diastereomers in good chemical yields from (-)-8-(benzylamino)menthol **1**,^[13] in three steps, as summarized in Scheme 2. Condensation of the amino alcohol **1** with ethyl glyoxylate in toluene at reflux furnished a mixture of equatorial **2a** and axial **2b** esters in 85:15 ratio which could be separated by silica column chromatography. However, **2b** is quite configurationally unstable and quickly reverts to **2a**.^[14] Treatment of either **2a** or the epimeric mixture of **2a** and **2b** with vinylic or allylic Grignard reagents gave the same equatorial carbinols **3a-d** that were converted into the final perhydrobenzoxazines **4a-g** by allylation the hydroxyl group.

Initial experiments were conducted on perhydro-1,3-benzoxazine **4a** with monosubstituted olefinic appendages. Reactions were carried out in CH_2Cl_2 at room temperature. In the presence of a 4 mol% of the first-generation Grubbs' catalyst **5**, **4a** was converted in a mixture of dihydrofurans **7a** and **8a** in good yield and moderate diastereoselectivity (entry 1 in Table 1). Employment of the Grubbs' second generation catalyst **6** resulted in a reverse stereoinduction,^[15] but the stereoselectivity remained moderate (entry 2 in Table 1).

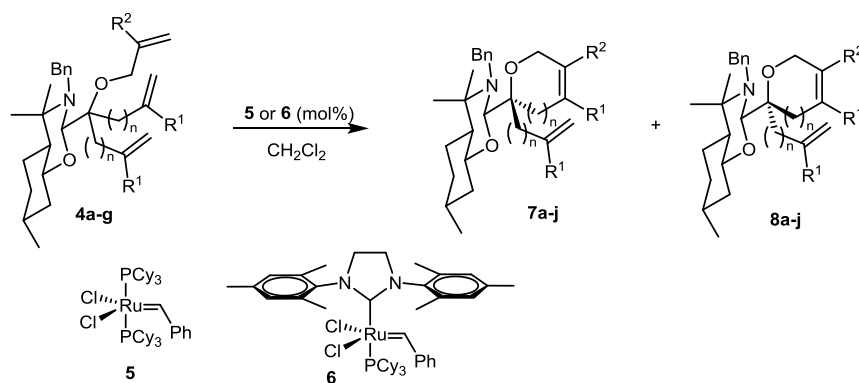
Although it is conceivable that the difference in the product ratios of the cyclization in the presence of **5**



Scheme 2. Synthesis of perhydrobenzoxazines **4a-g**.

or **6** reflect a kinetic or thermodynamic preference, it is quite unlikely that the reaction of **4a** with the most active ruthenium(II)-N-heterocyclic carbene complex **6** will take under thermodynamic rather than kinetic control in the tested reaction conditions for several reasons: (i) the product ratios do not change with time; for example, the reaction of **4a** in the presence of **6** for 30 h led to **7a** (35%) and **8a** (65%), almost the same ratio of diastereomers as after 55 h (entry 3); (ii) running the reaction in CH_2Cl_2 at 40 °C or in toluene at 110 °C for 30 h resulted in partial degradation of the material without any significant change in the diastereoselectivity (entries 4 and 5); (iii) once isolated, diastereomers **7a** and **8a** do not interconvert when subjected to the reaction conditions even in ethylene atmosphere. We believe that this catalyst-specificity is attributed to the different spatial arrangements of the respective ligands during the cyclization.

In a similar way triene **4e** with monosubstituted olefinic appendages provided dihydropyran **7e** as major isomer in the presence of **5** and dihydropyran **8e** in the presence of **6** (entries 11 and 12). When the first-generation Grubbs' catalyst **5** was used, the cyclopentene resulting from RCM reaction of the diastereotopic olefin chains was also isolated in a 20% yield. This compound was also formed initially when the second-generation Grubbs' catalyst **6** was used but over time it was transformed in a mixture of **7e** and **8e** by a rearrangement involving a diastereoselective ring-opening metathesis reaction. As with **4a**, a detailed monitoring of the reaction of **4e** in the presence of **6** showed that proportion of diastereoisomers **7e** and **8e** do not change with

Table 1. DSRCM reaction of trienes **4a-g**.

Entry	4	n	R ¹	R ²	T. (°C)	Catalyst (mol) ^[a]	t (h) ^[a]	Yield (%) ^[b]	dr (%) ^[c]
1	4a	0	H	H	20	5 (2 + 2)	15 + 10	89	7a (64)/ 8a (36)
2	4a	0	H	H	20	6 (2 + 2)	15 + 15	79	7a (35)/ 8a (65)
3	4a	0	H	H	20	6 (2 + 2 + 2)	15 + 15 + 25	56	7a (33)/ 8a (67)
4	4a	0	H	H	40	6 (2 + 2)	15 + 15	68	7a (33)/ 8a (67)
5	4a	0	H	H	110 ^[d]	6 (2 + 2)	15 + 15	55	7a (32)/ 8a (68)
6	4b	0	H	Me	40	5 (2 + 2)	15 + 10	--- ^[e]	---
7	4b	0	H	Me	40	6 (2 + 2)	15 + 15	30 ^[e]	7b (47)/ 8b (53)
8	4c	0	Me	H	40	5 (2 + 2)	15 + 15	53 ^[e]	7c (>98) ^[f]
9	4c	0	Me	H	20	6 (2)	12	92	7c (>98) ^[f]
10	4d	0	Me	Me	40	6 (2 + 2 + 2)	15 + 15 + 10	86	7d (83)/ 8d (17)
11	4e	1	H	H	20	5 (2)	15	75	7e (77)/ 8e (23)
12	4e	1	H	H	20	6 (2)	15	96	7e (36)/ 8e (64)
13	4f	1	Me	H	20	5 (2)	12	94	7f (78)/ 8f (22)
14	4f	1	Me	H	20	6 (2)	12	93	7f (36)/ 8f (64)
15	4g	1	Me	Me	40	6 (2 + 2 + 2)	15 + 15 + 10	84	7g (72)/ 8g (28)

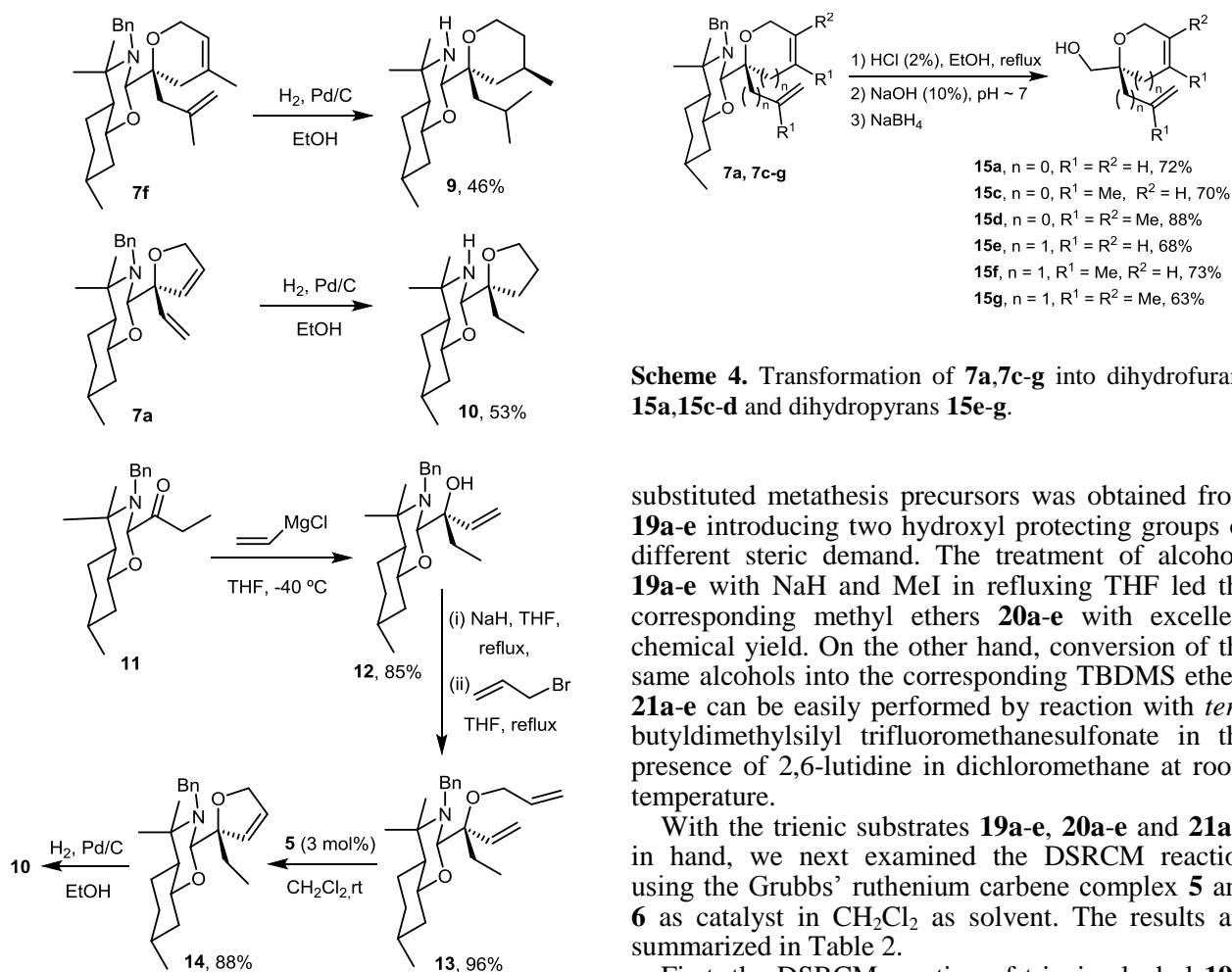
^[a] Catalyst was replenished after the time indicated in the Table; see also Experimental Section. ^[b] Yield refers to pure compounds after column chromatography. ^[c] Determined by ¹H NMR on the reaction mixtures. ^[d] Toluene was used as solvent. ^[e] Different amounts of the starting materials were recovered. ^[f] Only one diastereomer was detected by ¹H NMR spectra of the reaction mixture.

reaction time. The low diastereoselectivity observed in the cyclization of **4a** and **4e** is presumably due to competing initiation at the various olefinic sites.

The effect of olefin substitution on stereoselectivity was studied in trienes **4b-d** and **4f-g** (entries 6-10 and 13-15). Triene **4b** with two diastereotopic vinyl chains and a 1,1-disubstituted olefinic chain cyclized with difficulty only in the presence of the most active catalyst **6** and with almost no diastereoselectivity (entries 6-7). On the contrary, the reaction of DRCM occurred with greater diastereoselectivity and better chemical yields when the two diastereotopic olefinic chains are 1,1-disubstituted at the double bond. Even dihydrofurans and dihydropyrans with a tetrasubstituted double bond can be prepared with good chemical yield in the presence of **6** (entries 10 and 15). The best result in terms of diastereoselectivity was obtained in the cyclization of **4c** which gave rise to the formation of a single diastereomer **7c**, in the presence of both **5** and **6** (entries 8 and 9).

The diastereomers formed in each reaction were isolated and purified by flash chromatography and the

absolute configuration of the newly created stereocentres in **7c**, **8d**, **8e** and **8g** was established by X-ray diffraction studies.^[16] On the other hand, the absolute configuration of the newly created stereocentre in **7f** was determined by its conversion into the perhydro-1,3-benzoxazine **9** by hydrogenation of the double bonds and hydrogenolysis of the benzyl group (Scheme 3), and X-ray diffraction analysis.^[16] In the same way hydrogenation of **7a** led to perhydro-1,3-benzoxazine **10**. Unfortunately, **10** turned out to be an oil that does not crystallize. However, **10** can be synthesized by another way that allows to determine without ambiguity its absolute stereochemistry (Scheme 3). The treatment of the ketone **11**^[14] with vinylmagnesium chloride provided the alcohol **12**. The absolute configuration in the newly created stereocentre was assigned as *R* in agreement with Eliel's reports.^[13,14] O-Allylation of alcohol **12** followed of RCM reaction and hydrogenation led to **10**.



Scheme 4. Transformation of **7a,7c-g** into dihydrofurans **15a,15c-d** and dihydropyrans **15e-g**.

substituted metathesis precursors was obtained from **19a-e** introducing two hydroxyl protecting groups of different steric demand. The treatment of alcohols **19a-e** with NaH and MeI in refluxing THF led the corresponding methyl ethers **20a-e** with excellent chemical yield. On the other hand, conversion of the same alcohols into the corresponding TBDMS ethers **21a-e** can be easily performed by reaction with *tert*-butyldimethylsilyl trifluoromethanesulfonate in the presence of 2,6-lutidine in dichloromethane at room temperature.

With the trienic substrates **19a-e**, **20a-e** and **21a-e** in hand, we next examined the DSRCM reaction using the Grubbs' ruthenium carbene complex **5** and **6** as catalyst in CH_2Cl_2 as solvent. The results are summarized in Table 2.

First, the DSRCM reaction of trienic alcohol **19a**, with monosubstituted olefinic appendages, in the presence of **5** was examined but, low conversion to cyclic products **22a** and **23a** and moderate diastereoselectivity was observed (entry 1 in Table 2). In the presence of the most active ruthenium carbene **6** a reversal of the stereoinduction occurred but the conversion and stereoselectivity remained moderate (entry 2).

The low conversion to cyclic products, even in the presence of high amounts of catalyst, 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.^[19] To avoid the formation of unreactive chelates we tested the protonation of perhydrobenzoxazine **19a**.^[20] However, treatment of the hydrochloride salt of **19a** with 4 mol-% of Grubbs' catalyst **5**, followed by a basic workup, gave the desired cyclic products **22a** and **23a** with only a slight improvement in the conversion and unfortunately, as an almost equal mixture of diastereomers (entry 3). To our delight, the ruthenium carbenes **5** and **6** promoted efficient ring closure of the methyl ether **20a** and the silyl ether **21a** (entries 4-7). The best results in terms of diastereoselectivity were achieved with the bulkier *tert*-butyldimethylsilyl protecting group. In the presence of the Grubbs' ruthenium carbene complex **6** perhydrobenzoxazine **21a** led to **26a** and **27a** in a ratio of 13:87 (entry 7).

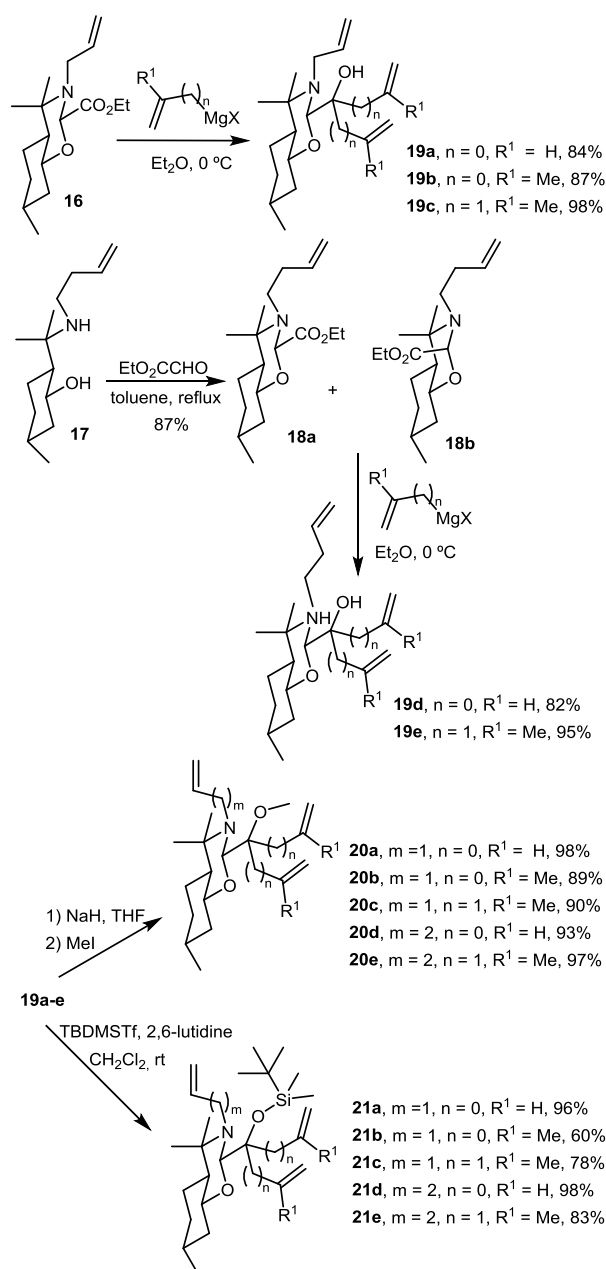
Scheme 3. Transformation of **7f** and **7a** into **9** and **10** and synthesis of **10** from **11**

The utility of these DSRCM reactions was demonstrated by the transformation of some products into the final enantiopure dihydrofurans **15a**, **15c** and **15d** and dihydropyrans **15e-g** which was achieved in moderate chemical yield as depicted in Scheme 4 by hydrolysis of the N,O-acetal moiety by treatment with dilute (~2%) aqueous alcoholic hydrochloric acid^[13] followed by reduction of the resulting aldehyde with sodium borohydride.

Synthesis of chiral cyclic amines

The starting trienic perhydro-1,3-benzoxazines **19a-e**, **20a-e**, and **21a-e** were prepared in good to excellent yields, as summarized in Scheme 5. Addition of vinylic or allylic Grignard reagents to perhydrobenzoxazine **16**^[12] led to the alcohols **19a-c**. Condensation of the amino alcohol **17**^[17] with ethyl glyoxylate in toluene at reflux furnished a mixture of equatorial **18a** and axial **18b** esters in 76:24 ratio. Treatment of either **18a** or the epimer **18b** with vinylic or allylic Grignard reagents gave the same equatorial carbinols **19d-e**.

Since protection of the hydroxyl group could be important to achieve optimal chemical yield and diastereoselectivity in the DSRCM reaction of hydroxyl-containing trienic substrates,^[18] a set of



Scheme 5. Synthesis of perhydrobenzoxazines **19a-e**, **20a-e** and **21a-e**.

Neither the trienic alcohol **19b** nor the corresponding silyl ether **21b** with two 1,1-disubstituted diastereotopic olefinic chains cyclized to the tetrahydropyridine ring (entries 8 and 11). The referable methyl ether **20b** failed also to cyclize if the catalyst used is **5** (entry 9), however, in the presence of **6**, cyclized easily to a mixture of diastereomeric tetrahydropyridines **24b** and **25b** with a trisubstituted double bond with good diastereoselectivity (92:8, entry 10).

Similarly, tetrahydro-1*H*-azepines can be prepared by DSRM reaction of trienes **19c**, **20c**, **21c**, **20d** and **21d** (entries 12-22). Again, the best results in terms of stereoselectivity were achieved when the hydroxyl group was protected as methyl ether if the diastereotopic olefin chains are 1,1-disubstituted

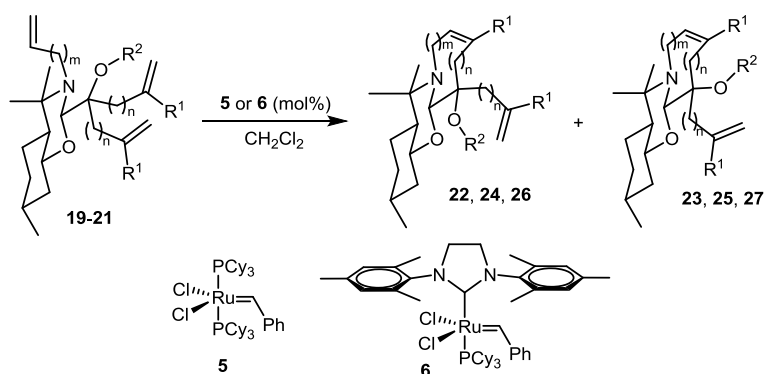
entries 14 and 15) or as *tert*-butyldimethylsilyl ether if the diastereotopic olefin chains are monosubstituted (entries 21 and 22). In both cases, only the formation of a single diastereomer was detected by ^1H NMR spectra of the reaction mixture.

More interesting, the ruthenium carbene **6** catalyzed the DSRM reaction of substrates **19e**, **20e** and **21e** providing the eight-membered cyclic amines (entries 23-25). As in **19c**, the OH group in **19e** does not seem to play a detrimental role in the diastereoselectivity (entry 23). Starting from the methyl ether **20e**, the corresponding hexahydroazocine **24e** with a trisubstituted double bond was obtained with good chemical yield and an excellent diastereoselectivity of 97: 3 (entry 24).

After isolation and purification by flash chromatography of the diastereomers formed in each reaction, the absolute configuration of the newly created stereocenters in **25a**, **24c** and **27d** was established by X-ray diffraction studies.^[16] The absolute configuration of the newly created stereocenters in **24e** was determined by its conversion into the aminomenthol derivatives **28** by nucleophilic ring opening of the N,O-acetal moiety by aluminum hydride (Scheme 6) and X-ray diffraction analysis.^[16] On the other hand, the NOESY spectra of **24b** showed a cross signal for the hydrogen attached to the N,O-acetalic carbon of the oxazine ring and the hydrogens of the methoxy group indicating their *cis* relationship and that, therefore, the absolute configuration of the new stereocenter created at the DSRM reaction is *R*.

On the other hand, O-methylation of **23a** provided **25a**, while the *tert*-butyldimethylsilyl ether cleavage of an inseparable mixture of **26a** and **27a** (13:87) with tetrabutylammonium fluoride in THF^[21] furnished a mixture of **22a** and **23a** in a 15:85 ratio, which allowed the assignment of the absolute stereochemistry of **25a**, **27a** and their epimers **24a** and **26a** respectively. In a similar way, the absolute configuration of the other RCM reaction products of Table 2 was assigned. Methylation of **22c** provided **24c**, while deprotection of *tert*-butyldimethylsilyl ether in **27c** furnished alcohol **23c**. Deprotection of silyl ether in **27d** followed by methylation of the resulting alcohol led **25d**. Last, methylation of **22e** provided **24e**, while the *tert*-butyldimethylsilyl ether cleavage of an inseparable mixture of **26e** and **27e** in a 45:55 ratio furnished a mixture of the epimeric azocines **22e** and **23e** in 41:59 ratio.

Transformation of compounds **25a**, **24b**, **22c**, **24c**, **25d** and **24e** into the final enantiopure tetrahydropyridines **29** and **33**, the tetrahydro-1*H*-azepines **30**, **32** and **34** and the hexahydroazocine **32** was performed in three steps,^[22] as depicted in Scheme 7. The reductive ring-opening of the N,O-acetal moiety by treatment with aluminium hydride generated in situ from lithium aluminium hydride and aluminium chloride, in THF at room temperature led to amino menthol derivatives in good to excellent yields. For a complete reduction of **24b** was

Table 2. DSRCM reaction of trienes **21-23**.

Entry		m	n	R ¹	R ²	T (°C)	Catalyst (mol) ^[a]	t (h) ^[a]	Yield (%) ^[b]	dr (%) ^[c]
1	19a	1	0	H	H	40	5 (2 + 2 + 2 + 2)	15 + 15 + 15 + 10	27 ^[d]	22a (64)/ 23a (36)
2	19a	1	0	H	H	40	6 (2 + 2 + 2)	15 + 15 + 10	38 ^[d]	22a (35)/ 23a (65)
3	19a·HCl	1	0	H	H	20	5 (2 + 2)	15 + 50	45 ^[d]	22a (48)/ 23a (52)
4	20a	1	0	H	Me	20	5 (2 + 2)	15 + 15	90	24a (67)/ 25a (33)
5	20a	1	0	H	Me	20	6 (2 + 2)	15 + 10	85	24a (27)/ 25a (73)
6	21a	1	0	H	TBDMS	20	5 (2 + 2)	15 + 15	83	26a (74)/ 27a (26)
7	21a	1	0	H	TBDMS	20	6 (2 + 2)	15 + 15	88	26a (13)/ 27a (87)
8	19b	1	0	Me	H	40	6 (2 + 2)	15 + 12	--- ^[d]	---
9	20b	1	0	Me	Me	40	5 (2 + 2)	15 + 15 + 10	--- ^[d]	---
10	20b	1	0	Me	Me	40	6 (2 + 2)	15 + 12	81	24b (92)/ 25b (8)
11	21b	1	0	Me	TBDMS	40	6 (2 + 2)	15 + 12	--- ^[d]	---
12	19c	1	1	Me	H	40	5 (2 + 2 + 2 + 2)	15 + 15 + 15 + 10	78	22c (92)/ 23c (8)
13	19c	1	1	Me	H	40	6 (2 + 2 + 2)	15 + 15 + 10	78	22c (73)/ 23c (27)
14	20c	1	1	Me	Me	40	5 (2 + 2)	15 + 10	94	24c (>98) ^[e]
15	20c	1	1	Me	Me	40	6 (2)	12	92	24c (>98) ^[e]
16	21c	1	1	Me	TBDMS	40	5 (2 + 2)	15 + 10	90	26c (35)/ 27c (65)
17	21c	1	1	Me	TBDMS	40	6 (2 + 2)	15 + 10	92	26c (12)/ 27c (88)
18	19d	2	0	H	H	20	6 (2 + 2)	15 + 10	--- ^[d]	---
19	20d	2	0	H	Me	20	5 (2 + 2)	15 + 10	91	24d (45)/ 25d (55)
20	20d	2	0	H	Me	20	6 (2)	12	85	24d (30)/ 25d (70)
21	21d	2	0	H	TBDMS	20	5 (2 + 2)	15 + 10	45	27d (>98) ^[e]
22	21d	2	0	H	TBDMS	20	6 (2 + 2)	15 + 10	94	27d (>98) ^[e]
23	19e	2	1	Me	H	40	6 (2 + 2 + 2)	15 + 15 + 10	52	22e (90)/ 23e (10)
24	20e	2	1	Me	Me	40	6 (3)	4	90	24e (97)/ 25e (3)
25	21e	2	1	Me	TBDMS	40	6 (3)	4	91	26e (45)/ 27e (55)

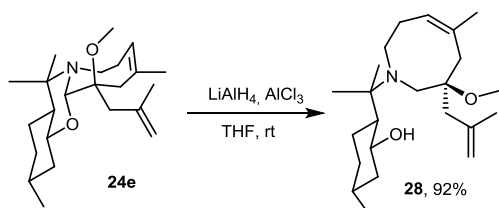
^[a] Catalyst was replenished after the time indicated in the Table; see also Experimental Section. ^[b] Yield refers to pure compounds after column chromatography. ^[c] Determined by ¹H NMR on the reaction mixtures. ^[d] Different amounts of the starting materials were recovered. ^[e] Only one diastereomer was detected by ¹H NMR spectra of the reaction mixture

necessary to heat to 60 °C and under these reaction conditions demethylation of the tertiary methyl ether also occurs. Elimination of the menthol appendage in these derivatives was effected by oxidation with PCC in CH₂Cl₂ at room temperature to the corresponding 8-aminomenthone derivatives followed by β-elimination by treatment with KOH in H₂O–THF–MeOH (Scheme 7).

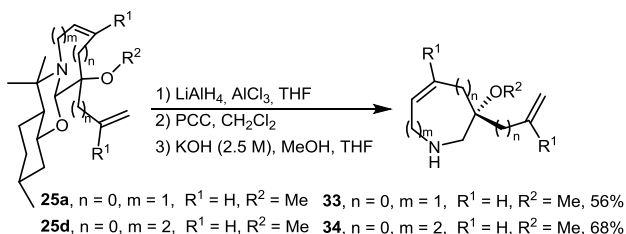
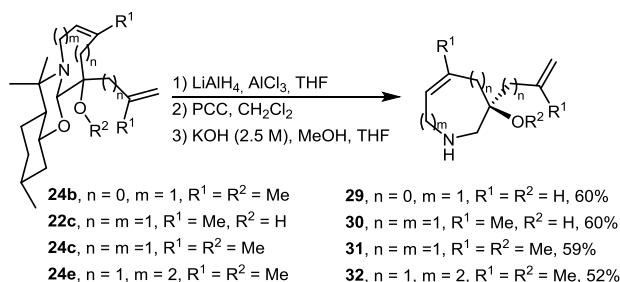
Conclusion

In summary, the synthetic sequence described above constitutes a short and efficient procedure for the

preparation of a variety of chiral oxygen- and nitrogen-containing heterocycles. The stereochemistry of the DSRCM reaction products is dependent on the length and position of the olefin chains in the perhydro-1,3-benzoxazine, the substitution pattern of the double bonds and the ruthenium carbene complex used as catalyst. The results collected in Table 1 and 2 show that the two catalysts, **5** and **6**, behave differently both in terms of efficiency and diastereoselectivities, leading to the opposite epimers for the final heterocycle except in the case of very high selectivity were reached, where the major product obtained with catalyst **6** correspond to the one which is mainly produced by catalyst **5**



Scheme 6. Stereochemical correlation of compound **24e**.



Scheme 7. Transformation of compounds **25a**, **24b**, **22c**, **24c**, **25d** and **24e** into the final enantiopure tetrahydropyridines **29** and **33**, the tetrahydro-1*H*-azepines **30**, **32** and **34**, and the hexahydroazocine **32**.

when the diastereoselectivity is moderate. In addition, the results seem to show that the substrate plays a major role in the selection of the final stereoisomer as compared to the catalyst. Although in some cases only moderate diastereoselectivities are achieved in the cyclization, after separation of the diastereomers and removal of the chiral auxiliary enantiopure oxygen- and nitrogen-containing heterocycles are obtained.

Experimental Section

General information

All reactions were carried out in anhydrous solvents, under an argon atmosphere, and in oven-dried glassware. Commercial reagents were used without purification. ¹H NMR (300 or 400 MHz) and ¹³C NMR (75 or 100 MHz) spectra were recorded in CDCl₃. Chemical shifts for protons are reported in ppm from tetramethylsilane with the residual CHCl₃ resonance as an internal reference. Chemical shifts for carbons are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t =

triplet, q = quartet, m = multiplet, br = broad), coupling constants in hertz, and integration. High resolution mass spectrometry (HRMS) analysis was performed using a quadrupole spectrometer equipped with a TOF analyzer. Specific rotations were measured using a 5 mL cell with a 1 dm path length and a sodium lamp, and the concentration is given in g per 100 mL. Melting points were determined in open capillary tubes and are uncorrected. Flash chromatography was carried out using silica gel (230–240 mesh). TLC analysis was performed on glass-backed plates coated with silica gel 60 and an F254 indicator, and visualized either by UV irradiation or by staining with I₂ or phosphomolybdic acid solution. Chemical yields refer to pure isolated substances. Compounds **1**,^[13] **11**,^[14] **16**,^[12] and **17**^[17] have been described previously. Compounds **2b**, **26a**, **27a**, **25b**, **26c**, **23e**, **26e** and **27e** could not be isolated and obtained pure after flash chromatography.

General procedure for the synthesis of benzoxazines 2 and 18. To a solution of 50 mmol of **1** or **17** in 150 mL of toluene was added 13 mL of a commercial solution of ethyl glyoxalate, 50% in toluene (65 mmol). The solution was heated at reflux with a Dean-Stark trap until disappearance of the starting material (TLC, 12–24 h). The solvent was removed *in vacuo* and the residue was chromatographed on silica gel using hexanes/AcOEt as an eluent.

Ethyl (2*S*,4*aS*,7*R*,8*aR*)-3-benzyl-4,4,7-trimethyloctahydro-2*H*-benzo[*e*][1,3]oxazine-2-carboxylate (2a**).** This compound was obtained from **1** (25.0 g) and purified by flash chromatography (hexanes/ethyl acetate 15:1) to give 20.37 g of **2a** and 9.33 g of a mixture of diastereomers **2a** and **2b** (90% yield). **2b** was quite configurationally unstable and quickly reverts to **2a**. White solid. Mp 81–82 °C (from hexane). [α]_D²⁵ = -51.6 (c = 0.7 ethyl acetate); ¹H NMR (400 MHz, CDCl₃): δ 0.93 (d, *J* = 6.5 Hz, 3H); 0.94–1.03 (m 2H); 0.98 (t, *J* = 7.2 Hz, 3H); 1.03 (s, 3H); 1.24 (m, 1H); 1.28 (s, 3H); 1.46 (m, 1H); 1.54–1.62 (m, 2H); 1.70 (m, 1H); 1.99 (m, 1H); 3.54 (td, *J*₁ = 10.5 Hz, *J*₂ = 4.0 Hz, 1H); 3.68 (dq, *J*₁ = 10.8 Hz, *J*₂ = 7.2 Hz, 1H); 3.85 (dq, *J*₁ = 10.8 Hz, *J*₂ = 7.2 Hz, 1H); 3.88 (d, *J* = 17.4 Hz, 1H); 3.95 (d, *J* = 17.4 Hz, 1H); 5.19 (s, 1H); 7.12 (t, *J* = 7.5 Hz, 1H); 7.22 (t, *J* = 7.5 Hz, 2H); 7.36 (d, *J* = 7.5 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 13.7 (CH₃); 20.7 (CH₃); 22.2 (CH₃); 24.9 (CH₃); 26.9 (CH₃); 31.4 (CH); 34.9 (CH₂); 41.1 (CH₂); 45.6 (CH); 48.1 (CH₂); 57.4 (C); 61.0 (CH₂); 76.3 (CH); 85.7 (CH); 126.1 (CH); 127.3 (2 CH); 127.7 (2 CH); 142.2 (C); 168.8 (C). IR (Nujol dispersion): 3080, 1750, 1600, 1255, 695 cm⁻¹. HRMS calcd for C₂₁H₃₂NO₃ [M + H]⁺ 346.2377, found 346.2373

Ethyl (2*S*,4*aS*,7*R*,8*aR*)-3-(but-3-en-1-yl)-4,4,7-trimethyloctahydro-2*H*-benzo[*e*][1,3]oxazine-2-carboxylate (18a**).** This compound was obtained from **17** (12.0 g) and purified by flash chromatography (hexanes/ethyl acetate 15:1). Yield: 10.83 g, 66%. Colorless oil. [α]_D²⁵ = -35.7 (c = 1.6 CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃): δ 0.88 (d, *J* = 6.5 Hz, 3H); 0.89–0.98 (m, 2H); 1.11 (m, 1H); 1.16 (s, 6H); 1.28 (t, *J* = 7.2 Hz, 3H); 1.35–1.48 (m, 2H); 1.56–1.69 (m, 2H); 1.93 (m, 1H); 2.08–2.17 (m, 2H); 2.57 (m, 1H); 2.71 (m, 1H); 3.46 (td, *J*₁ = 10.6 Hz, *J*₂ = 4.0 Hz, 1H); 4.14–4.32 (m, 2H); 4.88–4.98 (m, 2H); 5.04 (s, 1H); 5.79 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 14.1 (CH₃); 19.9 (CH₃); 22.1 (CH₃); 24.9 (CH₂); 26.1 (CH₃); 31.2 (CH); 34.8 (CH₂); 37.2 (CH₂); 40.9 (CH₂); 44.5 (CH₂); 45.6 (CH); 57.1 (C); 61.3 (CH₂); 76.0 (CH); 85.7 (CH); 115.3 (CH₂); 136.1 (CH); 169.0 (C). IR (pellicula): 3075, 1760, 1640, 910 cm⁻¹. HRMS calcd for C₁₈H₃₂NO₃ [M + H]⁺ 310.2377, found 310.2373.

Ethyl (2*R*,4*aS*,7*R*,8*aR*)-3-(but-3-en-1-yl)-4,4,7-trimethyloctahydro-2*H*-benzo[*e*][1,3]oxazine-2-carboxylate (18b**).** This compound was obtained from **17** (12.0 g) and purified by flash chromatography (hexanes/ethyl acetate 15:1). Yield: 3.42 g, 21%. Colorless oil. [α]_D²⁵ = +35.5 (c = 1.4 CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃): δ 0.88–1.09 (m, 3H); 0.93 (d, *J* = 6.5 Hz, 3H);

1.01 (s, 3H); 1.16 (s, 3H); 1.30 (t, $J = 7.1$ Hz, 3H); 1.39-1.60 (m, 2H); 1.63-1.75 (m, 2H); 1.99 (m, 1H); 2.20-2.32 (m, 2H); 2.88-3.01 (m, 2H); 3.94 (td, $J_1 = 10.6$ Hz, $J_2 = 4.0$ Hz, 1H); 4.18-4.25 (m, 2H); 4.80 (s, 1H); 4.98-5.09 (m, 2H); 5.82 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 14.0 (CH₃); 19.7 (CH₃); 22.1 (CH₃); 24.8 (CH₂); 27.5 (CH₃); 31.0 (CH); 34.7 (CH₂); 34.8 (CH₂); 41.2 (CH₂); 46.6 (CH₂); 47.9 (CH); 55.3 (C); 60.7 (CH₂); 70.7 (CH); 83.7 (CH); 115.6 (CH₂); 136.3 (CH); 172.6 (C). IR (film): 3075, 1740, 1640, 910 cm^{-1} . HRMS calcd for $\text{C}_{18}\text{H}_{32}\text{NO}_3$ [$\text{M} + \text{H}$]⁺ 310.2377, found 310.2377.

General procedure for addition of Grignard reagents to 2a, 11, 16 and the mixture of 18a and 18b. A commercial solution of the appropriate vinyl- or allyl-Grignard derivative in ether or THF (46 mmol) was slowly added at 0 °C to a solution of the appropriate benzoxazine (20 mmol) in diethyl ether (70 mL). The mixture was stirred at this temperature until disappearance of the starting material (TLC, 20-45 min). The reaction mixture was quenched with saturated ammonium chloride and the product was extracted with diethyl ether (3 x 40 mL). The organic extracts were washed with brine, dried over anhydrous MgSO_4 , and the solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel using hexanes/ AcOEt as an eluent.

For ketone **11**, the addition of vinyl magnesium chloride (1.2 eq) was carried out at -40 °C and THF was used as solvent instead of ether.

3-((2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)penta-1,4-dien-3-ol (3a).

This compound was obtained from **2a** (7.0 g) and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 5.96 g, 83%. Colorless oil. $[\alpha]_{\text{D}}^{25} = +1.8$ ($c = 0.9$ EtOH); ^1H NMR (300 MHz, CDCl_3): δ 0.89-1.04 (m, 2H); 0.96 (s, 3H); 0.97 (d, $J = 6.5$ Hz, 3H); 1.16 (m, 1H); 1.32 (s, 3H); 1.32-1.64 (m, 3H); 1.73 (m, 1H); 1.96 (m, 1H); 2.82 (s, 1H); 3.57 (dt, $J_1 = 10.5$ Hz, $J_2 = 4.0$ Hz, 1H); 3.85 (d, $J = 18.5$ Hz, 1H); 4.55 (d, $J = 18.5$ Hz, 1H); 4.72 (s, 1H); 4.99 (dd, $J_1 = 10.6$ Hz, $J_2 = 1.6$ Hz, 2H); 5.08 (dd, $J_1 = 17.3$ Hz, $J_2 = 1.6$ Hz, 1H); 5.22 (dd, $J_1 = 17.3$ Hz, $J_2 = 1.6$ Hz, 1H); 6.02 (ddd, $J_1 = 17.3$ Hz, $J_2 = 10.6$ Hz, $J_3 = 0.6$ Hz, 1H); 6.12 (dd, $J_1 = 17.3$ Hz, $J_2 = 10.6$ Hz, 1H); 7.16 (m, 1H); 7.25-7.34 (m, 4H). ^{13}C NMR (75 MHz, CDCl_3): δ 22.2 (CH₃); 22.9 (CH₃); 24.9 (CH₂); 26.6 (CH₃); 31.4 (CH); 35.1 (CH₂); 41.3 (CH₂); 44.6 (CH); 46.7 (CH₂); 58.6 (C); 76.1 (C); 77.9 (CH); 91.0 (CH); 112.7 (CH₂); 113.0 (CH₂); 125.6 (CH); 126.6 (2 CH); 127.9 (2 CH); 139.8 (CH); 140.2 (CH); 143.7 (C). IR (film): 3535 (broad), 3025, 1605, 760, 720, 695 cm^{-1} . HRMS calcd for $\text{C}_{23}\text{H}_{34}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 356.2584, found 356.2586

3-((2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)-2,4-dimethylpenta-1,4-dien-3-ol (3b).

This compound was obtained from **2a** (7.0 g) and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 6.22 g, 88%. Colorless oil. $[\alpha]_{\text{D}}^{25} = +22.5$ ($c = 0.9$ CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3): δ 0.77 (s, 3H); 0.79-1.05 (m, 2H); 0.94 (d, $J = 6.5$ Hz, 3H); 1.14 (m, 1H); 1.27 (m, 1H); 1.31 (s, 3H); 1.43-1.59 (m, 2H); 1.67 (s, 3H); 1.68 (m, 1H); 1.77 (s, 3H); 1.85 (m, 1H); 3.00 (s, 1H); 3.61 (dt, $J_1 = 10.6$ Hz, $J_2 = 3.9$ Hz, 1H); 3.78 (d, $J = 17.6$ Hz, 1H); 4.66 (t, $J = 1.5$ Hz, 1H); 4.92-5.01 (m, 4H); 5.23 (s, 1H); 7.11 (m, 1H); 7.19-7.27 (m, 4H). ^{13}C NMR (75 MHz, CDCl_3): δ 18.9 (CH₃); 19.4 (CH₃); 22.2 (CH₃); 22.5 (CH₃); 24.8 (CH₂); 27.3 (CH₃); 31.4 (CH); 35.1 (CH₂); 41.3 (CH₂); 43.3 (CH); 47.5 (CH₂); 58.6 (C); 77.0 (CH); 80.5 (C); 85.2 (CH); 110.8 (CH₂); 113.1 (CH₂); 124.9 (CH); 126.6 (2 CH); 127.1 (2 CH); 141.3 (C); 145.5 (C); 147.6 (C). IR (film): 3550 (broad), 3085, 2868, 1640, 1605, 750, 720, 695 cm^{-1} . HRMS calcd for $\text{C}_{25}\text{H}_{38}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 384.2897, found 384.2900.

3-((2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)-2,4-dimethylpenta-1,4-dien-3-ol (3c).

This compound was obtained from **2a** (3.6 g) and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 3.61 g, 90%. White solid. Mp 82-84

°C (from hexane). $[\alpha]_{\text{D}}^{25} = +62.0$ ($c = 0.8$ CH_2Cl_2); ^1H NMR (300 MHz, CDCl_3): δ 0.80-0.93 (m, 2H); 0.87 (s, 3H); 0.94 (d, $J = 6.5$ Hz, 3H); 1.09 (m, 1H); 1.25 (s, 3H); 1.52-1.68 (m, 4H); 1.92 (m, 1H); 2.24-2.40 (m, 4H); 2.43 (s, 1H); 3.51 (td, $J_1 = 10.4$ Hz, $J_2 = 3.9$ Hz, 1H); 3.88 (d, $J = 18.3$ Hz, 1H); 4.50 (s, 1H); 4.96 (d, $J = 18.3$ Hz, 1H); 5.02-5.08 (m, 4H); 5.78-6.00 (m, 2H); 7.11 (m, 1H); 7.19-7.22 (m, 2H); 7.36-7.39 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ 22.3 (CH₃); 22.7 (CH₃); 24.9 (CH₂); 26.9 (CH₃); 31.5 (CH); 35.2 (CH₂); 38.7 (CH₂); 41.4 (CH₂); 43.6 (CH₂); 43.9 (CH); 47.1 (CH₂); 58.4 (C); 75.6 (C); 77.6 (CH); 88.0 (CH); 118.0 (CH₂); 118.1 (CH₂); 125.4 (CH); 126.7 (2 CH); 127.8 (2 CH); 134.0 (CH); 134.2 (CH); 144.4 (C). IR (Nujol dispersion): 3399 (broad), 3070, 1720, 1640, 720, 695 650 cm^{-1} . HRMS calcd for $\text{C}_{25}\text{H}_{38}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 384.2897, found 384.2905.

4-((2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)-2,6-dimethylhepta-1,6-dien-4-ol (3d).

This compound was obtained from a mixture of **2a** and **2b** (7.0 g) and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 7.64 g, 92%. Colorless oil. $[\alpha]_{\text{D}}^{25} = +14.3$ ($c = 1.4$ CH_2Cl_2); ^1H NMR (300 MHz, CDCl_3): δ 0.79-0.98 (m, 2H); 0.89 (s, 3H); 0.94 (d, $J = 6.5$ Hz, 3H); 1.11 (m, 1H); 1.26 (s, 3H); 1.26-1.67 (m, 4H); 1.68 (s, 3H); 1.77 (s, 3H); 1.85 (m, 1H); 2.20 (d, $J = 14.9$ Hz, 1H); 2.22 (d, $J = 14.9$ Hz, 1H); 2.32 (d, $J = 14.9$ Hz, 2H); 2.68 (s, 1H); 3.49 (td, $J_1 = 10.6$ Hz, $J_2 = 4.0$ Hz, 1H); 3.91 (d, $J = 18.5$ Hz, 1H); 4.59 (s, 1H); 4.66-4.84 (m, 5H); 7.13 (m, 1H); 7.23-7.32 (m, 2H); 7.39-7.41 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3): δ 22.4 (CH₃); 22.8 (CH₃); 24.7 (CH₃); 24.7 (CH₃); 24.9 (CH₂); 26.9 (CH₃); 31.5 (CH); 35.2 (CH₂); 41.3 (CH₂); 43.4 (CH₂); 44.0 (CH); 47.2 (CH₂); 47.4 (CH₂); 58.7 (C); 76.5 (C); 77.0 (CH); 88.4 (CH); 113.5 (CH₂); 114.1 (CH₂); 125.5 (CH); 126.8 (2 CH); 127.9 (2 CH); 143.4 (C); 143.8 (C); 147.6 (C). IR (film): 3545 (broad), 3070, 2870, 1640, 720, 695 650 cm^{-1} . HRMS calcd for $\text{C}_{27}\text{H}_{42}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 412.3210, found 412.3212.

(R)-3-((2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)penta-1-en-3-ol (12).

This compound was obtained from **11** (2.5 g) and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 2.30 g, 85%. White solid. Mp 118-119 °C (from hexane). $[\alpha]_{\text{D}}^{25} = +8.9$ ($c = 1.1$ CH_2Cl_2); ^1H NMR (300 MHz, CDCl_3): δ 0.82 (t, $J = 7.4$ Hz, 3H); 0.88 (m, 2H); 0.94 (d, $J = 6.5$ Hz, 3H); 0.96 (s, 3H); 1.14 (m, 1H); 1.33 (s, 3H); 1.43-1.68 (m, 5H); 1.70 (m, 1H); 1.91 (m, 1H); 2.50 (s, 1H); 3.53 (td, $J_1 = 10.5$ Hz, $J_2 = 3.8$ Hz, 1H); 3.83 (d, $J = 18.6$ Hz, 1H); 4.61 (d, $J = 18.6$ Hz, 1H); 4.67 (s, 1H, CH); 4.94 (d, $J = 17.1$ Hz, 1H); 4.95 (d, $J = 11.1$ Hz, 1H); 5.97 (dd, $J_1 = 17.1$ Hz, $J_2 = 11.1$ Hz, 1H); 7.13 (m, 1H); 7.24-7.32 (m, 4H). ^{13}C NMR (75 MHz, CDCl_3): δ 7.53 (CH₃); 22.3 (CH₃); 22.9 (CH₃); 24.9 (CH₂); 26.6 (CH₃); 31.4 (CH and CH₂); 35.1 (CH₂); 41.3 (CH₂); 44.6 (CH); 46.8 (CH₂); 58.3 (C); 76.0 (C); 78.0 (CH); 90.9 (CH); 113.1 (CH₂); 125.6 (CH); 126.3 (2 CH); 128.1 (2 CH); 140.8 (CH); 143.9 (C). IR (film): 3540 (broad), 3025, 1605, 765, 725, 695 cm^{-1} . HRMS calcd for $\text{C}_{23}\text{H}_{36}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 358.2741, found 358.2746

3-((2S,4aS,7R,8aR)-3-allyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)penta-1,4-dien-3-ol (19a).

This compound was obtained from **16** (10.0 g) and purified by flash chromatography (hexanes/ethyl acetate 45:1). Yield: 8.70 g, 84%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -42.8$ ($c = 1.4$ CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3): δ 0.84-0.94 (m, 2H); 0.92 (d, $J = 6.2$ Hz, 3H); 1.06 (m, 1H); 1.09 (s, 3H); 1.21 (s, 3H); 1.43-1.51 (m, 2H); 1.58 (m, 1H); 1.69 (m, 1H); 1.90 (m, 1H); 2.97 (s, 1H); 3.24 (dd, $J_1 = 18.3$ Hz, $J_2 = 4.9$ Hz, 1H); 3.47 (td, $J_1 = 10.6$ Hz, $J_2 = 3.9$ Hz, 1H); 3.79 (dd, $J_1 = 18.3$ Hz, $J_2 = 4.9$ Hz, 1H); 4.56 (s, 1H); 4.97-5.17 (m, 4H); 5.32 (dd, $J_1 = 12.8$ Hz, $J_2 = 1.7$ Hz, 1H); 5.38 (dd, $J_1 = 12.8$ Hz, $J_2 = 1.7$ Hz, 1H); 5.85 (m, 1H); 6.00 (dd, $J_1 = 17.3$ Hz, $J_2 = 10.8$ Hz, 1H); 6.15 (dd, $J_1 = 17.3$ Hz, $J_2 = 10.8$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 22.2 (CH₃); 22.8 (CH₃); 24.9 (CH₂); 26.3 (CH₃); 31.4 (CH); 35.1 (CH₂); 41.2 (CH₂); 45.0 (CH); 45.3 (CH₂); 58.0 (C); 75.7 (C); 77.9 (CH); 90.7 (CH); 112.5 (2 CH₂); 113.5

(CH₂); 140.1 (CH); 140.6 (CH); 141.4 (CH). IR (film): 3524 (broad), 3085, 1640, 820, 720, 635 cm⁻¹. HRMS calcd for C₁₉H₃₂NO₂ [M + H]⁺ 306.2428, found 306.243

3-((2S,4aS,7R,8aR)-3-allyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)-2,4-dimethylpenta-1,4-dien-3-ol (19b). This compound was obtained from **16** (10.0 g) and purified by flash chromatography (hexanes/ethyl acetate 45:1). Yield: 9.80 g, 87%. Colorless oil. [α]_D²⁵ = +8.3 (c = 1.0 CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.90-1.00 (m, 2H); 0.92 (d, J = 6.5 Hz, 3H); 1.05 (m, 1H); 1.07 (s, 3H); 1.23 (s, 3H); 1.43-1.62 (m, 3H); 1.69 (s, 6H); 1.71 (m, 1H); 1.88 (m, 1H); 3.02 (s, 1H); 3.34 (dd, J₁ = 17.4 Hz, J₂ = 6.4 Hz, 1H); 3.53 (td, J₁ = 10.6 Hz, J₂ = 3.9 Hz, 1H); 4.05 (dd, J₁ = 17.4 Hz, J₂ = 4.3 Hz, 1H); 4.79-4.98 (m, 5H); 5.06 (s, 1H); 5.21 (m, 1H); 5.89 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 19.0 (CH₃); 19.1 (CH₃); 22.2 (CH₃); 22.6 (CH₃); 25.0 (CH₂); 27.1 (CH₃); 31.4 (CH); 35.2 (CH₂); 41.4 (CH₂); 44.4 (CH); 46.9 (CH₂); 58.3 (C); 77.0 (CH); 80.3 (C); 85.5 (CH); 110.9 (CH₂); 111.3 (CH₂); 112.0 (CH₂); 142.8 (CH); 143.5 (CH); 147.4 (CH). IR (film): 3550 (broad), 3085, 1640, 735, 610 cm⁻¹. HRMS calcd for C₂₁H₃₆NO₂ [M + H]⁺ 334.2741, found 334.2748.

4-((2S,4aS,7R,8aR)-3-allyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)-2,6-dimethylhepta-1,6-dien-4-ol (19c). This compound was obtained from **16** (10.0 g) and purified by flash chromatography (hexanes/ethyl acetate 45:1). Yield: 12.02 g, 98%. Colorless oil. [α]_D²⁵ = -25.3 (c = 1.8 CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.83-0.94 (m, 2H); 0.92 (d, J = 6.5 Hz, 3H); 0.99 (m, 1H); 1.07 (s, 3H); 1.17 (s, 3H); 1.43-1.68 (m, 3H); 1.70-1.70-1.76 (m, 2H); 1.81 (s, 3H); 1.83 (s, 3H); 2.18 (d, J = 14.6 Hz, 1H); 2.27 (d, J = 14.6 Hz, 1H); 2.33 (d, J = 14.6 Hz, 1H); 2.45 (d, J = 14.6 Hz, 1H); 2.69 (s, 1H); 3.33 (dd, J₁ = 18.3 Hz, J₂ = 5.5 Hz, 1H); 3.41 (td, J₁ = 10.6 Hz, J₂ = 3.9 Hz, 1H); 4.07 (dd, J₁ = 18.3 Hz, J₂ = 4.7 Hz, 1H); 4.44 (s, 1H); 4.72-4.88 (m, 4H); 4.99 (dd, J₁ = 10.4 Hz, J₂ = 1.9 Hz, 1H); 5.15 (dd, J₁ = 17.5 Hz, J₂ = 1.9 Hz, 1H); 5.95 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 22.0 (CH₃); 22.5 (CH₃); 24.3 (CH₃); 24.4 (CH₃); 24.7 (CH₂); 26.6 (CH₃); 31.1 (CH); 34.9 (CH₂); 41.0 (CH₂); 43.1 (CH₂); 43.9 (CH); 45.6 (CH₂); 47.0 (CH₂); 58.0 (C); 75.9 (CH); 76.5 (C); 87.7 (CH); 113.0 (CH₂); 113.2 (CH₂); 114.0 (CH₂); 141.5 (CH); 143.2 (C). IR (film): 3550 (broad), 3070, 1640, 735 cm⁻¹. HRMS calcd for C₂₃H₄₀NO₂ [M + H]⁺ 362.3054, found 362.3057.

3-((2S,4aS,7R,8aR)-3-(but-3-en-1-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)penta-1,4-dien-3-ol (19d). This compound was obtained from **18a** (9.30 g) and purified by flash chromatography (hexanes/ethyl acetate 45:1). Yield: 7.90 g, 82%. Colorless oil. [α]_D²⁵ = -47.3 (c = 1.2 CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.85-0.94 (m, 2H); 0.91 (d, J = 6.6 Hz, 3H); 1.06 (m, 1H); 1.15 (s, 3H); 1.18 (s, 3H); 1.48-1.52 (m, 2H); 1.57 (m, 1H); 1.69 (m, 1H); 1.90 (m, 1H); 2.08-2.21 (m, 2H); 2.46 (m, 1H); 3.05 (m, 1H); 3.14 (s, 1H); 3.44 (td, J₁ = 10.5 Hz, J₂ = 4.0 Hz, 1H); 4.49 (s, 1H); 4.91-4.99 (m, 2H); 5.07 (dd, J₁ = 10.5 Hz, J₂ = 1.8 Hz, 1H); 5.10 (dd, J₁ = 10.5 Hz, J₂ = 1.8 Hz, 1H); 5.37 (dd, J₁ = 17.1 Hz, J₂ = 1.8 Hz, 1H); 5.48 (dd, J₁ = 17.1 Hz, J₂ = 1.8 Hz, 1H); 5.61 (m, 1H); 6.02 (dd, J₁ = 17.1 Hz, J₂ = 10.5 Hz, 1H); 6.15 (dd, J₁ = 17.1 Hz, J₂ = 10.5 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 22.1 (CH₃); 22.9 (CH₃); 24.8 (CH₂); 26.1 (CH₃); 31.3 (CH); 34.9 (CH₂); 37.4 (CH₂); 41.0 (CH₂); 42.2 (CH₂); 44.5 (CH); 57.8 (C); 74.9 (C); 77.9 (CH); 91.1 (C); 112.0 (CH₂); 112.1 (CH₂); 115.2 (CH₂); 135.8 (CH); 139.4 (CH); 141.1 (CH). IR (film): 3460 (broad), 3075, 1640, 735, 630 cm⁻¹. HRMS calcd for C₂₀H₃₄NO₂ [M + H]⁺ 320.2584, found 320.2584.

4-((2S,4aS,7R,8aR)-3-(but-3-en-1-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazin-2-yl)-2,6-dimethylhepta-1,6-dien-4-ol (19e). This compound was obtained from a mixture of **18a** and **18b** (5.5 g) and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 6.64 g, 95%. Colorless oil. [α]_D²⁵ = -26.5 (c =

1.4 CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.85-0.96 (m, 2H); 0.92 (d, J = 6.5 Hz, 3H); 0.97-1.02 (m, 1H); 1.14 (s, 6H); 1.21-1.51 (m, 2H); 1.59 (m, 1H); 1.68-1.79 (m, 2H); 1.84 (s, 3H); 1.85 (s, 3H); 2.21-2.44 (m, 6H); 2.63 (m, 1H); 2.77 (s, 1H); 3.07 (m, 1H); 3.39 (td, J₁ = 10.5 Hz, J₂ = 3.9 Hz, 1H); 4.46 (s, 1H); 4.73-4.90 (m, 4H); 4.95 (dd, J₁ = 10.3 Hz, J₂ = 1.9 Hz, 1H); 5.02 (dd, J₁ = 17.2 Hz, J₂ = 1.9 Hz, 1H); 5.75 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 22.3 (CH₃); 22.9 (CH₃); 24.6 (CH₃); 24.7 (CH₃); 25.0 (CH₂); 26.7 (CH₃); 31.4 (CH); 35.2 (CH₂); 38.0 (CH₂); 41.2 (CH₂); 42.9 (CH₂); 44.0 (CH₂); 44.3 (CH); 46.4 (CH₂); 58.4 (C); 75.7 (C); 77.0 (CH); 88.0 (CH); 113.7 (CH₂); 114.4 (CH₂); 115.2 (CH₂); 136.6 (CH); 143.4 (C); 143.7 (C). IR (film): 3548 (broad), 3075, 1640, 730 cm⁻¹. HRMS calcd for C₂₄H₄₂NO₂ [M + H]⁺ 376.3210, found 376.3209.

General procedure for O-allylation of alcohols 3a-d and 12. To a solution of alcohol **3a-d** or **12** (8.0 mmol) in THF (40 mL) was added NaH (60% dispersion in mineral oil, 0.96 g, 24 mmol). The mixture was heated to reflux for 20 min and cooled to ambient temperature. Allyl bromide or methallyl bromide (10.4 mmol) was added, and the mixture was again refluxed until the starting material was fully consumed as indicated by TLC. After aqueous workup, the THF was evaporated and the aqueous residue was extracted with diethyl ether (3 x 30 mL). The organic extracts were washed with brine, dried over anhydrous MgSO₄, and the solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel using hexanes/AcOEt as an eluent.

(2S,4aS,7R,8aR)-2-(3-(allyloxy)penta-1,4-dien-3-yl)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (4a). This compound was obtained from **3a** (2.8 g) and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 3.04 g, 98%. Colorless oil. [α]_D²⁵ = -18.5 (c = 1.6 CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.84-0.95 (m, 2H); 0.86 (s, 3H); 0.94 (d, J = 6.5 Hz, 3H); 1.12 (m, 1H); 1.25 (s, 3H); 1.32-1.57 (m, 3H); 1.69 (m, 1H); 1.96 (m, 1H); 3.53 (td, J₁ = 10.5 Hz, J₂ = 3.9 Hz, 1H); 3.83 (d, J = 18.4 Hz, 1H); 3.89-4.00 (m, 2H); 4.59 (d, J = 18.4 Hz, 1H); 4.75 (s, 1H); 5.04-5.17 (m, 6H); 5.84-6.06 (m, 3H); 7.11 (m, 1H); 7.20-7.25 (m, 2H); 7.34-7.37 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 22.2 (CH₃); 22.5 (CH₃); 22.8 (CH₂); 26.8 (CH₃); 31.4 (CH); 35.1 (CH₂); 41.4 (CH₂); 44.1 (CH); 47.5 (CH₂); 58.2 (C); 64.4 (CH₂); 77.6 (CH); 82.1 (C); 91.7 (CH); 114.8 (2 CH₂); 116.7 (CH₂); 125.2 (CH); 127.1 (2 CH); 127.4 (2 CH); 135.9 (CH); 137.6 (CH); 137.9 (CH); 144.2 (C). IR (film): 3080, 2980, 1635, 1450, 720, 695 cm⁻¹. HRMS calcd for C₂₆H₃₈NO₂ [M + H]⁺ 396.2897, found 396.2900.

(2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyl-2-(3-((2-methylallyl)oxy)penta-1,4-dien-3-yl)octahydro-2H-benzo[e][1,3]oxazine (4b). This compound was obtained from **3a** (2.8 g) and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 2.75 g, 85%. Colorless oil. [α]_D²⁵ = -9.3 (c = 1.3 CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.83-0.96 (m, 2H); 0.84 (s, 3H); 0.94 (d, J = 6.5 Hz, 3H); 1.15 (m, 1H); 1.26 (s, 3H); 1.46-1.72 (m, 4H); 1.66 (s, 3H); 1.96 (m, 1H); 3.53 (td, J₁ = 10.5 Hz, J₂ = 3.9 Hz, 1H); 3.80-3.90 (m, 3H); 4.58 (d, J = 18.0 Hz, 1H); 4.78 (s, 1H); 4.79 (d, J = 1.1 Hz, 1H); 5.03-5.31 (m, 5H); 5.89-6.06 (m, 2H); 7.14 (m, 1H); 7.22-7.24 (m, 2H); 7.34-7.37 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 19.6 (CH₃); 22.2 (CH₃); 22.5 (CH₃); 24.8 (CH₂); 26.8 (CH₃); 31.3 (CH); 35.1 (CH₂); 41.3 (CH₂); 44.0 (CH); 47.5 (CH₂); 58.2 (C); 66.8 (CH₂); 77.5 (CH); 81.9 (C); 91.7 (CH); 109.6 (CH₂); 114.7 (CH₂); 116.7 (CH₂); 125.1 (CH); 127.0 (2 CH); 127.4 (2 CH); 137.6 (CH); 137.9 (CH); 143.1 (C); 144.2 (C). IR (film): 3080, 2925, 1650, 1450, 720, 700 cm⁻¹. HRMS calcd for C₂₇H₄₀NO₂ [M + H]⁺ 410.3054, found 410.3054.

(2S,4aS,7R,8aR)-2-(3-(allyloxy)-2,4-dimethylpenta-1,4-dien-3-yl)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (4c). This compound was obtained from **3b** (3.0 g) and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 2.90 g, 88%. Colorless

oil. $[\alpha]_{\text{D}}^{25} = -18.6$ ($c = 1.3 \text{ CH}_2\text{Cl}_2$). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 0.78 (s, 3H); 0.88-0.98 (m, 2H); 0.96 (d, $J = 6.6$ Hz, 3H); 1.04 (m, 1H); 1.29 (s, 3H); 1.54-1.55 (m, 2H); 1.57 (s, 3H); 1.66-1.75 (m, 2H); 1.78 (s, 3H); 1.83 (m, 1H); 3.47 (td, $J_1 = 10.5$ Hz, $J_2 = 3.9$ Hz, 1H); 3.84 (d, $J = 17.5$ Hz, 1H); 3.95 (dd, $J_1 = 14.2$ Hz, $J_2 = 4.6$ Hz, 1H); 4.44 (dd, $J_1 = 14.2$ Hz, $J_2 = 4.6$ Hz, 1H); 4.76 (s, 1H); 5.01-5.30 (m, 7H); 5.93 (m, 1H); 7.10 (m, 1H); 7.18-7.23 (m, 2H); 7.27-7.34 (m, 2H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 19.4 (CH₃); 19.9 (CH₃); 22.3 (CH₃); 22.4 (CH₃); 24.9 (CH₂); 27.5 (CH₃); 31.5 (CH); 35.3 (CH₂); 41.6 (CH₂); 43.3 (CH); 47.3 (CH₂); 58.7 (C); 66.6 (CH₂); 77.0 (CH); 85.5 (C); 87.5 (CH); 113.8 (CH₂); 113.9 (CH₂); 115.3 (CH₂); 124.8 (CH); 127.1 (2 CH); 127.1 (2 CH); 137.0 (CH); 142.3 (C); 143.8 (C); 146.1 (C). IR (film): 3060, 2945, 1640, 1450, 720, 695 cm^{-1} . HRMS calcd for $\text{C}_{28}\text{H}_{42}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 424.3210, found 424.3214.

(2S,4aS,7R,8aR)-3-benzyl-2-(2,4-dimethyl-3-((2-methylallyl)oxy)penta-1,4-dien-3-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (4d). This compound was obtained from **3b** (3.1 g) and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 3.29 g, 93%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -20.9$ ($c = 1.0 \text{ CH}_2\text{Cl}_2$). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 0.76 (s, 3H); 0.82-0.99 (m, 2H); 0.94 (d, $J = 6.6$ Hz, 3H); 1.12 (m, 1H); 1.27 (s, 3H); 1.52-1.76 (m, 4H); 1.54 (s, 3H); 1.70 (s, 3H); 1.75 (s, 3H); 1.88 (m, 1H); 3.45 (td, $J_1 = 10.5$ Hz, $J_2 = 3.9$ Hz, 1H); 3.80 (d, $J = 14.0$ Hz, 1H); 3.82 (d, $J = 17.1$ Hz, 1H); 4.37 (d, $J = 14.0$ Hz, 1H); 4.73 (d, $J = 1.1$ Hz, 2H); 4.92 (d, $J = 1.1$ Hz, 1H); 5.07-5.17 (m, 4H); 5.20 (s, 1H); 7.07 (m, 1H); 7.15-7.20 (m, 2H); 7.24-7.31 (m, 2H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 19.4 (CH₃); 19.9 (2 CH₃); 22.3 (2 CH₃); 24.9 (CH₂); 27.4 (CH₃); 31.5 (CH); 35.3 (CH₂); 41.6 (CH₂); 43.3 (CH); 47.2 (CH₂); 58.6 (C); 69.0 (CH₂); 77.0 (CH); 85.3 (C); 87.7 (CH); 109.2 (CH₂); 113.9 (CH₂); 115.3 (CH₂); 124.8 (CH_{ar}); 127.0 (2 CH); 127.1 (2 CH); 142.4 (C); 143.8 (C); 144.1 (C); 146.0 (C). IR (film): 3065, 2915, 1635, 1450, 720, 695 cm^{-1} . HRMS calcd for $\text{C}_{29}\text{H}_{44}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 438.3367, found 438.3377.

(2S,4aS,7R,8aR)-2-(4-(allyloxy)hepta-1,6-dien-4-yl)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (4e). This compound was obtained from **3c** (3.1 g) and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 3.15 g, 92%. Colorless oil. $[\alpha]_{\text{D}}^{25} = +40.6$ ($c = 1.7 \text{ CH}_2\text{Cl}_2$). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 0.82-1.01 (m, 2H); 0.89 (s, 3H); 0.96 (d, $J = 6.5$ Hz, 3H); 1.12 (m, 1H); 1.24 (s, 3H); 1.43-1.62 (m, 3H); 1.70 (m, 1H); 1.92 (m, 1H); 2.27 (dd, $J_1 = 14.0$ Hz, $J_2 = 6.9$ Hz, 1H); 2.36 (dd, $J_1 = 14.0$ Hz, $J_2 = 7.4$ Hz, 1H); 2.43 (dd, $J_1 = 14.4$ Hz, $J_2 = 8.5$ Hz, 1H); 2.67 (dd, $J_1 = 14.4$ Hz, $J_2 = 5.4$ Hz, 1H); 3.37 (td, $J_1 = 10.4$ Hz, $J_2 = 4.0$ Hz, 1H); 3.92 (d, $J = 18.4$ Hz, 1H); 4.07 (dd, $J_1 = 13.2$ Hz, $J_2 = 5.1$ Hz, 1H); 4.43 (dd, $J_1 = 13.2$ Hz, $J_2 = 5.3$ Hz, 1H); 4.48 (s, 1H); 4.95-5.16 (m, 7H); 5.75-5.98 (m, 3H); 7.14 (m, 1H); 7.21-7.27 (m, 2H); 7.31-7.45 (m, 2H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 22.3 (CH₃); 22.4 (CH₃); 24.8 (CH₂); 26.7 (CH₃); 31.3 (CH₂); 35.1 (CH₂); 37.0 (CH₂); 39.4 (CH₂); 41.6 (CH₂); 43.9 (CH); 46.6 (CH₂); 58.3 (C); 64.8 (CH₂); 77.5 (CH); 80.3 (C); 89.9 (CH); 114.5 (CH₂); 117.6 (2 CH₂); 125.1 (CH); 126.5 (2 CH); 127.6 (2 CH); 134.2 (CH); 134.6 (CH); 136.1 (CH); 144.8 (C). IR (film): 3075, 2925, 1640, 1450, 725, 695 cm^{-1} . HRMS calcd for $\text{C}_{28}\text{H}_{42}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 424.3210, found 424.3217.

(2S,4aS,7R,8aR)-2-(4-(allyloxy)-2,6-dimethylhepta-1,6-dien-4-yl)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (4f). This compound was obtained from **3d** (3.2 g) and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 3.37 g, 96%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -5.1$ ($c = 1.2 \text{ CH}_2\text{Cl}_2$). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 0.86-0.98 (m, 2H); 0.90 (s, 3H); 0.94 (d, $J = 6.5$ Hz, 3H); 1.11 (m, 1H); 1.22 (s, 3H); 1.35-1.56 (m, 3H); 1.60 (s, 3H); 1.72 (m, 1H); 1.82 (s, 3H); 1.88 (m, 1H); 2.23 (d, $J = 15.0$ Hz, 1H); 2.40 (d, $J = 14.1$ Hz, 1H); 2.56 (d, $J = 15.0$ Hz, 1H); 2.69 (d, $J = 14.1$ Hz, 1H); 3.36 (td, $J_1 = 10.5$ Hz, $J_2 = 4.0$ Hz, 1H); 3.92 (d, $J = 18.2$ Hz, 1H); 4.14 (dd, $J_1 = 13.2$ Hz, $J_2 = 4.9$ Hz, 1H); 4.49 (dd, $J_1 = 13.2$ Hz, $J_2 = 5.1$ Hz, 1H); 4.58 (s, 1H); 4.81 (s, 2H); 4.90 (s, 2H); 4.91-

5.06 (m, 2H); 5.83 (m, 1H); 7.11 (m, 1H); 7.21-7.27 (m, 2H); 7.40-7.42 (m, 2H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 22.3 (CH₃); 22.6 (CH₃); 24.9 (CH₂); 25.1 (2CH₃); 26.8 (CH₃); 31.4 (CH); 35.2 (CH₂); 38.7 (CH₂); 41.5 (CH₂); 42.0 (CH₂); 44.0 (CH); 46.7 (CH₂); 58.6 (C); 64.7 (CH₂); 77.0 (CH); 82.0 (C); 89.8 (CH); 114.0 (CH₂); 114.4 (CH₂); 114.6 (CH₂); 125.1 (CH); 126.9 (2 CH); 127.6 (2 CH); 136.4 (CH); 142.7 (C); 143.6 (C); 145.0 (C). IR (film): 3075, 2920, 1640, 1450, 720, 670 cm^{-1} . HRMS calcd for $\text{C}_{30}\text{H}_{46}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 452.3523, found 452.3532.

(2S,4aS,7R,8aR)-3-benzyl-2-(2,6-dimethyl-4-((2-methylallyl)oxy)hepta-1,6-dien-4-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (4g). This compound was obtained from **3d** (3.1 g) and purified by flash chromatography (hexanes/ethyl acetate 55:1). Yield: 3.26 g, 93%. Colorless oil. $[\alpha]_{\text{D}}^{25} = +2.3$ ($c = 1.7 \text{ CH}_2\text{Cl}_2$). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 0.85-1.01 (m, 2H); 0.90 (s, 3H); 0.94 (d, $J = 6.5$ Hz, 3H); 1.14 (m, 1H); 1.22 (s, 3H); 1.35-1.61 (m, 2H); 1.59 (s, 3H); 1.66 (s, 3H); 1.68 (m, 1H); 1.83 (s, 3H); 1.89 (m, 1H); 2.22 (d, $J = 15.0$ Hz, 1H); 2.38 (d, $J = 13.9$ Hz, 1H); 2.57 (d, $J = 15.0$ Hz, 1H); 2.74 (d, $J = 13.9$ Hz, 1H); 3.35 (td, $J_1 = 10.5$ Hz, $J_2 = 3.9$ Hz, 1H); 3.91 (d, $J = 18.3$ Hz, 1H); 3.99 (d, $J = 12.7$ Hz, 1H); 4.40 (d, $J = 12.7$ Hz, 1H); 4.59 (s, 1H); 4.72 (d, $J = 0.9$ Hz); 4.79 (s, 1H); 4.80 (s, 1H); 4.83 (s, 1H); 4.90 (s, 1H); 5.00 (d, $J = 18.3$ Hz, 1H); 7.17 (m, 1H); 7.31-7.40 (m, 2H); 7.2-7.47 (m, 2H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 20.1 (CH₃); 22.3 (CH₃); 22.6 (CH₃); 24.9 (CH₂); 25.1 (CH₃); 25.2 (CH₃); 26.8 (CH₃); 31.4 (CH); 35.2 (CH₂); 38.6 (CH₂); 41.6 (CH₂); 42.1 (CH₂); 44.0 (CH); 46.7 (CH₂); 58.5 (C); 67.3 (CH₂); 76.9 (CH); 82.0 (C); 89.8 (CH); 110.0 (CH₂); 114.0 (CH₂); 114.7 (CH₂); 125.0 (CH); 126.9 (2 CH); 127.5 (2 CH); 142.8 (C); 143.6 (C); 143.7 (C); 145.0 (C). IR (film): 3075, 1640, 720, 695 cm^{-1} . HRMS calcd for $\text{C}_{31}\text{H}_{48}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 466.3680, found 466.3687.

(2S,4aS,7R,8aR)-2-((R)-3-(allyloxy)pent-1-en-3-yl)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (13). This compound was obtained from **12** (2.2 g) and purified by flash chromatography (hexanes/ethyl acetate 45:1). Yield: 2.35 g, 96%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -11.3$ ($c = 1.3 \text{ CH}_2\text{Cl}_2$). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 0.8 (t, $J = 7.4$ Hz, 3H); 0.87 (s, 3H); 0.89-1.11 (m, 2H); 0.94 (d, $J = 6.5$ Hz, 3H); 1.17 (m, 1H); 1.28 (s, 3H, CH₃); 1.42-1.63 (m, 3H); 1.64-1.73 (m, 3H); 1.90 (m, 1H); 3.46 (td, $J_1 = 10.6$ Hz, $J_2 = 3.7$ Hz, 1H); 3.82 (d, $J = 17.9$ Hz, 1H); 4.14 (m, 1H); 4.34 (m, 1H); 4.76 (s, 1H); 4.84 (d, $J = 17.9$ Hz, 1H); 5.03-5.14 (m, 2H); 5.14-5.25 (m, 2H); 5.85-5.95 (m, 2H); 7.11 (m, 1H); 7.19-7.24 (m, 2H); 7.36-7.39 (m, 2H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 7.4 (CH₃); 22.3 (2CH₃); 24.9 (CH₂); 27.1 (CH₃); 28.1 (CH₂); 35.5 (CH); 35.2 (CH₂); 41.5 (CH₂); 44.1 (CH); 47.5 (CH₂); 58.3 (C); 63.8 (CH₂); 77.8 (CH); 80.5 (C); 90.0 (CH); 114.6 (CH₂); 115.0 (CH₂); 125.1 (CH); 127.0 (2 CH); 127.5 (2 CH); 136.3 (CH); 138.9 (CH); 144.2 (C). IR (film): 3064, 1452, 721, 695 cm^{-1} . HRMS calcd for $\text{C}_{26}\text{H}_{40}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 398.3054, found 398.3054.

General procedure for methylation of alcohols 19a-e. To a solution of alcohols **19a-e** (9.0 mmol) in THF (45 mL) was added NaH (60% dispersion in mineral oil, 1.1 g, 27 mmol). The mixture was heated to reflux for 20 min and cooled to ambient temperature. Iodomethane (1.8 mL, 28.8 mmol) was added, and the mixture was again refluxed until the starting material was fully consumed as indicated by TLC. After aqueous workup, the THF was evaporated and the aqueous residue was extracted with ethyl acetate (3 x 40 mL). The organic extracts were washed with brine, dried over anhydrous MgSO_4 , and the solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel using hexanes/AcOEt as an eluent.

(2S,4aS,7R,8aR)-3-allyl-2-(3-methoxy-penta-1,4-dien-3-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (20a). This compound was obtained from **19a** (2.75 g) and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 2.82 g, 98%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -49.2$ ($c = 1.2 \text{ CH}_2\text{Cl}_2$). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 0.86-0.96 (m,

2H); 0.91 (d, $J = 6.5$ Hz, 3H); 1.07 (s, 3H); 1.10 (m, 1H); 1.16 (s, 3H); 1.21-1.57 (m, 3H); 1.68 (m, 1H); 1.93 (m, 1H); 3.19 (s, 3H); 3.32 (dd, $J_1 = 17.9$ Hz, $J_2 = 5.3$ Hz, 1H); 3.45 (td, $J_1 = 10.6$ Hz, $J_2 = 3.9$ Hz, 1H); 3.83 (dd, $J_1 = 17.9$ Hz, $J_2 = 5.3$ Hz, 1H); 4.57 (s, 1H); 4.91 (dd, $J_1 = 10.3$ Hz, $J_2 = 1.9$ Hz, 1H); 5.03 (dd, $J_1 = 17.4$ Hz, $J_2 = 1.9$ Hz, 1H); 5.20-5.34 (m, 4H); 5.85-6.05 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 22.1 (CH₃); 22.5 (CH₃); 24.9 (CH₂); 26.4 (CH₂); 31.3 (CH); 35.1 (CH₂); 41.3 (CH₂); 44.7 (CH); 46.4 (CH₂); 51.4 (CH₃); 57.8 (C); 77.4 (CH); 82.0 (C); 91.3 (CH); 112.7 (CH₂); 115.2 (CH₂); 117.2 (CH₂); 136.9 (CH); 137.9 (CH); 141.8 (CH). IR (film): 3085, 1635, 830 cm^{-1} . HRMS calcd for $\text{C}_{20}\text{H}_{34}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 320.2584, found 320.2587.

(2S,4aS,7R,8aR)-3-allyl-2-(3-methoxy-2,4-dimethylpenta-1,4-dien-3-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (20b). This compound was obtained from **19b** (3.0 g) and purified by flash chromatography (hexanes/ethyl acetate 75:1). Yield: 2.80 g, 89%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -5.8$ ($c = 1.0$ CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3): δ 0.87-0.94 (m, 2H); 0.92 (d, $J = 6.5$ Hz, 3H); 1.05 (m, H); 1.06 (s, 3H); 1.18 (s, 3H); 1.26-1.55 (m, 2H); 1.57 (s, 3H); 1.65 (s, 3H); 1.69 (m, 1H); 1.86 (m, 1H); 3.31-3.48 (m, 2H); 3.38 (s, 3H); 4.16 (dd, $J_1 = 17.3$ Hz, $J_2 = 4.5$ Hz, 1H); 4.77-4.94 (m, 3H); 5.02 (s, 1H); 5.13-6.00 (m, 3H); 6.04 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 19.6 (CH₃); 19.8 (CH₃); 22.3 (CH₃); 22.4 (CH₃); 25.1 (CH₂); 27.2 (CH₃); 31.5 (CH); 35.2 (CH₂); 41.7 (CH₂); 44.4 (CH); 46.7 (CH₂); 53.9 (CH₃); 58.4 (C); 77.0 (CH); 85.5 (C); 87.7 (CH); 111.0 (CH₂); 112.5 (CH₂); 115.6 (CH₂); 143.4 (C); 143.9 (C); 144.3 (CH). IR (film): 3070, 1640, 830, 730 cm^{-1} . HRMS calcd for $\text{C}_{22}\text{H}_{38}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 348.2897, found 348.2900.

(2S,4aS,7R,8aR)-3-allyl-2-(4-methoxy-2,6-dimethylhepta-1,6-dien-4-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (20c). This compound was obtained from **19c** (3.0 g) and purified by flash chromatography (hexanes/ethyl acetate 75:1). Yield: 2.80 g, 90%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -41.4$ ($c = 1.0$ CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3): δ 0.86-0.96 (m, 2H); 0.91 (d, $J = 6.5$ Hz, 3H); 1.05 (m, 1H); 1.09 (s, 3H); 1.11 (s, 3H); 1.42-1.59 (m, 3H); 1.70 (m, 1H); 1.78 (s, 3H); 1.82 (s, 3H); 1.84 (m, 1H); 2.21 (d, $J = 15.0$ Hz, 1H); 2.42 (d, $J = 14.2$ Hz, 1H); 2.57 (d, $J = 15.0$ Hz, 1H); 2.64 (d, $J = 14.2$ Hz, 1H); 3.28 (td, $J_1 = 10.4$ Hz, $J_2 = 3.9$ Hz, 1H); 3.41 (s, 3H); 3.43 (dd, $J_1 = 17.7$ Hz, $J_2 = 5.4$ Hz, 1H); 4.11 (dd, $J_1 = 17.7$ Hz, $J_2 = 5.4$ Hz, 1H); 4.41 (s, 1H); 4.80-4.86 (m, 4H); 4.94 (dd, $J_1 = 10.3$ Hz, $J_2 = 1.9$ Hz, 1H); 5.10 (dd, $J_1 = 17.3$ Hz, $J_2 = 1.9$ Hz, 1H); 6.04 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 22.2 (CH₃); 22.4 (CH₃); 24.8 (CH₃); 24.9 (CH₂); 25.2 (CH₃); 26.8 (CH₂); 31.4 (CH); 35.2 (CH₂); 38.3 (CH₂); 41.4 (CH₂); 41.5 (CH₂); 44.3 (CH); 46.0 (CH₂); 51.2 (CH₃); 58.3 (C); 76.6 (CH); 81.5 (C); 89.6 (CH); 112.6 (CH₂); 114.1 (2 CH₂); 142.4 (CH); 142.7 (C); 143.1 (C). IR (film): 3075, 1640, 890, 785 cm^{-1} . HRMS calcd for $\text{C}_{24}\text{H}_{42}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 376.3210, found 376.3209.

(2S,4aS,7R,8aR)-3-(but-3-en-1-yl)-2-(3-methoxypenta-1,4-dien-3-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (20d). This compound was obtained from **19d** (3.0 g) and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 2.91 g, 93%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -69.6$ ($c = 1.4$ CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3): δ 0.88 (m, 2H); 0.90 (d, $J = 6.5$ Hz, 3H); 1.03 (m, 1H); 1.13 (s, 3H, CH₃); 1.16 (s, 3H, CH₃); 1.39-1.47 (m, 2H); 1.32 (m, 1H); 1.67 (m, 1H); 1.91 (m, 1H); 2.12 (m, 1H); 2.29 (m, 1H); 2.55 (m, 1H); 3.12 (m, 1H); 3.23 (s, 3H); 3.44 (td, $J_1 = 10.6$ Hz, $J_2 = 3.8$ Hz, 1H); 4.57 (s, 1H); 4.91 (dd, $J_1 = 9.9$ Hz, $J_2 = 2.0$ Hz, 1H); 4.96 (m, 1H); 5.22-5.35 (m, 4H); 5.66 (m, 1H); 5.96 (dd, $J_1 = 17.6$ Hz, $J_2 = 9.9$ Hz, 1H); 6.05 (dd, $J_1 = 17.6$ Hz, $J_2 = 9.9$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 22.2 (CH₃); 22.5 (CH₃); 25.1 (CH₂); 26.2 (CH₂); 31.4 (CH); 35.1 (CH₂); 37.3 (CH₂); 41.4 (CH₂); 43.0 (CH₂); 44.9 (CH); 51.4 (CH₃); 57.6 (C); 77.5 (CH); 81.5 (C); 90.8 (CH); 114.7 (CH₂); 115.0 (CH₂); 116.9 (CH₂); 136.9 (CH); 137.2 (CH); 140.0 (CH). IR (film): 3075, 1640, 1455, 915 cm^{-1} . HRMS calcd for $\text{C}_{21}\text{H}_{36}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 334.2741, found 334.2747.

(2S,4aS,7R,8aR)-3-(but-3-en-1-yl)-2-(4-methoxy-2,6-dimethylhepta-1,6-dien-4-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (20e). This compound was obtained from **19e** (2.1 g) and purified by flash chromatography (hexanes/ethyl acetate 80:1). Yield: 2.12 g, 97%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -52.6$ ($c = 1.2$ CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3): δ 0.84-0.91 (m, 2H); 0.90 (d, $J = 6.5$ Hz, 3H); 0.98 (m, 1H); 1.09 (s, 3H); 1.14 (s, 3H); 1.17-1.79 (m, 4H); 1.81 (s, 3H); 1.82 (s, 3H); 1.83 (m, 1H); 2.16 (d, $J = 14.4$ Hz, 1H); 2.25 (m, 1H); 2.44 (d, $J = 14.4$ Hz, 1H); 2.48-2.62 (m, 2H); 2.63 (d, $J = 14.4$ Hz, 1H); 2.69 (d, $J = 14.4$ Hz, 1H); 3.26 (td, $J_1 = 10.3$ Hz, $J_2 = 4.0$ Hz, 1H); 3.33 (m, 1H); 3.41 (s, 3H); 4.33 (s, 1H); 4.84-5.16 (m, 6H); 5.53 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 22.3 (CH₃); 22.6 (CH₃); 25.1 (2CH₃); 25.3 (CH₂); 26.5 (CH₃); 31.5 (CH); 35.2 (CH₂); 37.9 (CH₂); 38.2 (CH₂); 41.5 (CH₂); 41.8 (CH₂); 43.2 (CH₂); 44.5 (CH); 51.5 (CH₃); 58.2 (C); 76.9 (CH); 81.4 (C); 89.7 (CH); 114.1 (CH₂); 114.4 (CH₂); 114.6 (CH₂); 137.6 (CH); 142.8 (C); 143.4 (C). IR (film): 3075, 1640, 750 cm^{-1} . HRMS calcd for $\text{C}_{25}\text{H}_{44}\text{NO}_2$ [$\text{M} + \text{H}$]⁺ 390.3367, found 390.3376.

General procedure for silylation of alcohols 19a-e. To a solution of alcohols **19a-e** (4.5 mmol) and 2,6-lutidine (1.1 mL, 9.0 mmol) in anhydrous CH_2Cl_2 (25 mL) was dropwise added *tert*-butyldimethylsilyl-triflate (1.7 mL, 7.2 mmol). The solution was stirred at room temperature until the starting material was fully consumed as indicated by TLC (for total transformation of alcohols **19b**, **19c** and **19e** it was necessary to add an extra amount of 2,6-lutidine, 0.3 mL, and TBSOTf, 0.45 mL). The reaction liquid was diluted with CH_2Cl_2 (60 mL), then washed with water, aqueous saturated ammonium chloride solution and aqueous saturated sodium chloride solution, then dried over anhydrous magnesium sulphate and concentrated. The residue was purified through silica gel column chromatography using hexanes/ethyl acetate as an eluent.

(2S,4aS,7R,8aR)-3-allyl-2-(3-((*tert*-butyldimethylsilyloxy)penta-1,4-dien-3-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (21a). This compound was obtained from **19a** (1.4 g) and purified by flash chromatography (hexanes/ethyl acetate 100:1). Yield: 1.85 g, 96%. Colorless oil. $[\alpha]_{\text{D}}^{25} = -34.5$ ($c = 1.0$ CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3): δ 0.08 (s, 3H); 0.10 (s, 3H); 0.85-0.90 (m, 2H); 0.89 (s, 9H); 0.93 (d, $J = 6.5$ Hz, 3H); 1.04 (s, 3H); 1.08 (m, 1H); 1.14 (s, 3H); 1.42-1.58 (m, 3H); 1.69 (m, 1H); 1.90 (m, 1H); 3.25 (dd, $J_1 = 17.7$ Hz, $J_2 = 6.0$ Hz, 1H); 3.43 (td, $J_1 = 10.6$ Hz, $J_2 = 3.9$ Hz, 1H); 3.88 (dd, $J_1 = 17.7$ Hz, $J_2 = 5.0$ Hz, 1H); 4.45 (s, 1H); 4.85 (dd, $J_1 = 10.6$ Hz, $J_2 = 1.8$ Hz, 1H); 4.93 (dd, $J_1 = 17.4$ Hz, $J_2 = 1.8$ Hz, 1H); 5.11 (dd, $J_1 = 10.6$ Hz, $J_2 = 1.8$ Hz, 1H); 5.16 (dd, $J_1 = 10.6$ Hz, $J_2 = 1.8$ Hz, 1H); 5.28 (dd, $J_1 = 17.4$ Hz, $J_2 = 1.8$ Hz, 1H); 5.29 (dd, $J_1 = 17.4$ Hz, $J_2 = 1.8$ Hz, 1H); 5.89 (m, 1H); 6.06 (dd, $J_1 = 17.4$ Hz, $J_2 = 10.6$ Hz, 1H); 6.12 (dd, $J_1 = 17.4$ Hz, $J_2 = 10.6$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ -1.9 (2 CH₃); 18.7 (C); 22.4 (CH₃); 22.8 (CH₃); 25.0 (CH₂); 26.1 (3 CH₃); 26.9 (CH₃); 31.5 (CH); 35.2 (CH₂); 41.4 (CH₂); 41.5 (CH); 46.6 (CH₂); 57.9 (C); 77.3 (CH); 80.0 (C); 91.1 (CH); 112.2 (CH₂); 114.2 (CH₂); 114.5 (CH₂); 139.7 (CH); 141.3 (CH); 142.8 (CH). IR (film): 3080, 1635, 835, 780, 685 cm^{-1} . HRMS calcd for $\text{C}_{25}\text{H}_{46}\text{NO}_2\text{Si}$ [$\text{M} + \text{H}$]⁺ 420.3292, found 420.3292.

(2S,4aS,7R,8aR)-3-allyl-2-(3-((*tert*-butyldimethylsilyloxy)-2,4-dimethylpenta-1,4-dien-3-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (21b). This compound was obtained from **19b** (1.65 g) and purified by flash chromatography (hexanes/ CH_2Cl_2 3:1). Yield: 1.33 g, 60%. White solid. Mp 53-54 °C (from hexane). $[\alpha]_{\text{D}}^{25} = -2.0$ ($c = 1.0$ CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3): δ 0.07 (s, 3H); 0.23 (s, 3H); 0.87-1.05 (m, 2H); 0.91 (s, 9H, 3CH₃); 0.94 (d, 3H, $J = 6.5$ Hz); 1.02 (s, 3H); 1.16 (m, 1H); 1.20 (s, 3H); 1.38-1.60 (m, 3H); 1.64 (s, 6H); 1.73 (m, 1H); 1.87 (m, 1H); 3.12 (dd, $J_1 = 17.3$ Hz, $J_2 = 7.6$ Hz, 1H); 3.51 (td, $J_1 = 10.6$ Hz, $J_2 = 3.8$ Hz, 1H); 4.19 (m, 1H); 4.71 (m, 1H); 4.82-4.88 (m, 2H); 4.97 (s, 1H); 4.98-5.00 (m, 2H); 5.30 (m, 1H); 5.77 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ -3.7 (CH₃); -1.3 (CH₃); 18.1 (C); 19.4 (CH₃); 19.9 (CH₃); 22.4 (CH₃); 22.5 (CH₃); 25.1

(CH₂); 26.8 (3 CH₃); 27.9 (CH₃); 31.7 (CH); 35.3 (CH₂); 41.4 (CH₂); 43.8 (CH); 47.5 (CH₂); 58.4 (C); 76.9 (CH); 84.9 (CH); 85.5 (C); 110.2 (CH₂); 112.1 (CH₂); 113.7 (CH₂); 144.5 (CH); 144.7 (C); 146.4 (C). IR (nujol dispersion): 3070, 1638, 835, 687 cm⁻¹. HRMS calcd for C₂₇H₅₀NO₂Si [M + H]⁺ 448.3605, found 448.3617.

(2S,4aS,7R,8aR)-3-allyl-2-(4-((tert-butyl)dimethylsilyloxy)-2,6-dimethylhepta-1,6-dien-4-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (21c). This compound was obtained from **19c** (1.7 g) and purified by flash chromatography (hexanes/ethyl acetate 100:1). Yield: 1.75 g, 78%. Colorless oil. [α]_D²⁵ = -31.0 (c = 1.5 CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.12 (s, 3H); 0.22 (s, 3H); 0.86-1.04 (m, 2H); 0.89 (s, 9H); 0.94 (d, *J* = 6.5 Hz, 3H); 1.05 (s, 3H); 1.09 (m, 1H); 1.12 (s, 3H); 1.45-1.58 (m, 3H); 1.70 (m, 1H); 1.83 (s, 6H); 1.88 (m, 1H); 2.16 (d, *J* = 14.5 Hz, 1H); 2.52 (d, *J* = 13.8 Hz, 1H); 2.66 (d, 1H, *J* = 13.8 Hz); 2.68 (d, *J* = 14.5 Hz, 1H); 3.25 (dd, *J*₁ = 18.2 Hz, *J*₂ = 5.7 Hz, 1H); 3.39 (td, *J*₁ = 10.6 Hz, *J*₂ = 3.8 Hz, 1H); 4.41 (s, 1H); 4.42 (dd, *J*₁ = 18.2 Hz, *J*₂ = 4.2 Hz, 1H); 4.85-4.96 (m, 5H); 5.11 (dd, *J*₁ = 17.4 Hz, *J*₂ = 1.8 Hz, 1H); 5.98 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ -0.9 (2 CH₃); 19.1 (C); 22.4 (CH₃); 22.9 (CH₃); 25.0 (CH₂); 25.1 (CH₃); 26.2 (CH₃); 26.6 (3CH₃); 27.1 (CH₃); 31.5 (CH); 35.3 (CH₂); 41.3 (CH₂); 42.1 (CH₂); 43.7 (CH); 45.0 (CH₂); 46.4 (CH₂); 58.2 (C); 76.5 (CH); 81.9 (C); 86.9 (CH); 112.4 (CH₂); 114.6 (CH₂); 115.0 (CH₂); 142.7 (CH); 142.9 (2C). IR (film): 3075, 1640, 775, 700, 670 cm⁻¹. HRMS calcd for C₂₉H₅₄NO₂Si [M + H]⁺ 476.3918, found 476.3917.

(2S,4aS,7R,8aR)-3-(but-3-en-1-yl)-2-(3-((tert-butyl)dimethylsilyloxy)penta-1,4-dien-3-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (21d). This compound was obtained from **19d** (1.0 g) and purified by flash chromatography (hexanes/ethyl acetate 100:1). Yield: 1.33 g, 98%. Colorless oil. [α]_D²⁵ = -27.1 (c = 1.0 CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 0.09 (s, 6H), 0.84-0.95 (m, 2H), 0.89 (s, 9H), 0.90 (d, 3H, *J* = 6.5 Hz), 1.07 (m, 1H), 1.09 (s, 3H), 1.13 (s, 3H), 1.39-1.48 (m, 2H), 1.55 (m, 1H), 1.67 (m, 1H), 1.88 (m, 1H), 2.06 (m, 1H), 2.23 (m, 1H), 2.46 (m, 1H), 3.19 (m, 1H), 3.41 (td, *J*₁ = 10.4 Hz, *J*₂ = 3.8 Hz, 1H), 4.43 (s, 1H), 4.84-4.93 (m, 2H), 5.10 (d, *J* = 10.6 Hz, 1H), 5.15 (d, *J* = 10.6 Hz, 1H), 5.25-5.35 (m, 2H), 5.62 (m, 1H), 6.02 (dd, *J*₁ = 17.3 Hz, *J*₂ = 10.6 Hz, 1H), 6.14 (dd, *J*₁ = 17.3 Hz, *J*₂ = 10.6 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ -1.8 (2 CH₃); 18.3 (C); 22.4 (CH₃); 22.9 (CH₃); 25.2 (CH₂); 26.1 (3 CH₃); 26.4 (CH₃); 31.5 (CH); 35.3 (CH₂); 37.8 (CH₂); 41.4 (CH₂); 43.0 (CH₂); 44.4 (CH); 57.5 (C); 77.4 (CH); 79.9 (C); 91.1 (CH); 114.0 (CH₂); 114.2 (CH₂); 114.7 (CH₂); 137.0 (CH); 140.4 (CH); 141.3 (CH). IR (film): 3080, 2925, 1640, 1470, 1460, 835, 780, 685 cm⁻¹. HRMS calcd for C₂₆H₄₈NO₂Si [M + H]⁺ 434.3449, found 434.3456.

(2S,4aS,7R,8aR)-3-(but-3-en-1-yl)-2-(4-((tert-butyl)dimethylsilyloxy)-2,6-dimethylhepta-1,6-dien-4-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (21e). This compound was obtained from **19e** (1.14 g) and purified by flash chromatography (hexanes/ethyl acetate 100:1). Yield: 1.23 g, 83%. Colorless oil. [α]_D²⁵ = -35.3 (c = 1.5 CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.12 (s, 3H); 0.19 (s, 3H); 89-1.04 (m, 3H); 0.91 (s, 9H); 0.93 (d, 3H, *J* = 6.6 Hz); 1.08 (m, 1H); 1.10 (s, 3H); 1.12 (s, 3H); 1.32-1.62 (m, 3H); 1.71 (m, 1H); 1.82 (s, 3H); 1.84 (m, 1H); 1.89 (s, 3H); 2.17 (d, 1H, *J* = 14.6 Hz); 2.28 (m, 1H); 2.38-2.50 (m, 3H); -2.61-2.72 (m, 2H); 3.38 (td, 1H, *J*₁ = 10.6 Hz, *J*₂ = 3.6 Hz); 3.68 (m, 1H); 3.36 (s, 1H); 4.85-5.04 (m, 6H); 5.78 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ -0.91 (2 CH₃); 19.2 (C); 22.3 (CH₃); 23.0 (CH₃); 25.0 (CH₂); 25.1 (CH₃); 26.3 (CH₃); 26.6 (3CH₃); 26.8 (CH₃); 31.5 (CH); 35.2 (CH₂); 38.3 (CH₂); 41.2 (CH₂); 42.4 (CH₂); 43.1 (CH₂); 43.5 (CH); 45.0 (CH₂); 58.1 (C); 76.5 (CH); 81.8 (C); 87.1 (CH); 114.8 (2 CH₂); 115.0 (CH₂); 137.2 (CH); 142.9 (C); 143.0 (C). IR (film): 3080, 2950, 1640, 1460, 835, 775 cm⁻¹. HRMS calcd for C₃₀H₅₆NO₂Si [M + H]⁺ 490.4075, found 490.4078.

General procedure for DSRM Reaction of trienes 4a-g, 19a-e, 20a-e, 21a-e and diene 14. The triene (3 mmol) was dissolved in dry CH₂Cl₂ (90 mL) and argon was bubbled. Grubbs first- or second-generation catalyst (0.06 mmol) was added and the resulting mixture was stirred at room temperature or at reflux under argon. The reaction progress was monitored by TLC and additional portions of fresh catalyst were added after the times indicated in Tables 1 and 2. When the reaction was found to be complete the solvent was evaporated *in vacuo* and the residue was purified by flash chromatography on silica gel using mixtures of hexanes/ethyl acetate as eluent.

(2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyl-2-((R)-2-vinyl-2,5-dihydrofuran-2-yl)octahydro-2H-benzo[e][1,3]oxazine (7a). This compound was obtained from **4a** (1.2 g) and catalyst **5**, and purified by flash chromatography (hexanes/ethyl acetate 45:1). Yield: 0.62 g, 56%. Colorless oil. [α]_D²⁵ = -32.9 (c = 1.8, CHCl₃). ¹H NMR (300 MHz, CDCl₃): δ 0.84-1.02 (m, 2H), 0.87 (s, 3H); 0.93 (d, *J* = 6.5 Hz, 3H); 1.14 (m, 1H); 1.27 (s, 3H); 1.34-1.50 (m, 3H); 1.60 (m, 1H); 1.94 (m, 1H); 3.51 (td, *J*₁ = 10.5 Hz, *J*₂ = 3.9 Hz, 1H); 3.87 (d, *J* = 18.3 Hz, 1H); 4.45-4.52 (m, 2H); 4.58 (d, *J* = 18.3 Hz, 1H); 4.78 (s, 1H); 4.97 (dd, *J*₁ = 10.7 Hz, *J*₂ = 1.7 Hz, 1H); 5.02 (dd, *J*₁ = 17.3 Hz, *J*₂ = 1.7 Hz, 1H); 5.73-5.81 (m, 2H); 6.16 (dd, *J*₁ = 17.3 Hz, *J*₂ = 10.7 Hz, 1H); 7.14 (m, 1H); 7.21-7.30 (m, 2H); 7.36-7.71 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 22.3 (CH₃); 22.8 (CH₃); 25.0 (CH₂); 26.7 (CH₃); 31.4 (CH); 35.2 (CH₂); 41.4 (CH₂); 44.3 (CH); 47.2 (CH₂); 57.9 (C); 75.3 (CH₂); 77.4 (CH); 90.6 (CH); 93.5 (C); 113.3 (CH₂); 125.2 (CH); 126.6 (CH); 127.0 (2 CH); 127.5 (2 CH); 130.3 (CH); 138.7 (CH); 144.4 (C). IR (film): 3060, 1730, 720, 695 cm⁻¹. HRMS calcd for C₂₄H₃₄NO₂ [M + H]⁺ 368.2584, found 368.2586.

(2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyl-2-((S)-2-vinyl-2,5-dihydrofuran-2-yl)octahydro-2H-benzo[e][1,3]oxazine (8a). This compound was obtained from **4a** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ethyl acetate 45:1). Yield: 0.57 g, 51%. Colorless oil. [α]_D²⁵ = +1.9 (c = 0.5, ethyl acetate). ¹H NMR (300 MHz, CDCl₃): δ 0.86-1.03 (m, 2H); 0.88 (s, 3H); 0.92 (d, *J* = 6.5 Hz, 3H); 1.18 (m, 1H); 1.26 (s, 3H); 1.29-1.67 (m, 4H); 1.93 (m, 1H); 3.51 (td, *J*₁ = 10.7 Hz, *J*₂ = 3.5 Hz, 1H); 3.96 (d, *J* = 18.6 Hz, 1H); 4.37-4.53 (m, 2H); 4.42 (d, *J* = 18.6 Hz, 1H); 4.74 (s, 1H); 4.99 (dd, *J*₁ = 10.6 Hz, *J*₂ = 1.7 Hz, 1H); 5.16 (dd, *J*₁ = 17.3 Hz, *J*₂ = 1.7 Hz, 1H); 5.63 (m, 1H); 5.79 (m, 1H); 6.07 (dd, *J*₁ = 17.3 Hz, *J*₂ = 10.6 Hz, 1H); 7.13 (m, 1H); 7.20-7.25 (m, 2H); 7.32-7.61 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 22.0 (CH₃); 22.2 (CH₃); 24.9 (CH₂); 26.6 (CH₃); 31.4 (CH); 35.1 (CH₂); 41.4 (CH₂); 44.8 (CH); 46.9 (CH₂); 58.2 (C); 74.8 (CH₂); 77.8 (CH); 90.5 (CH); 94.0 (C); 113.0 (CH₂); 125.2 (CH); 126.7 (CH); 127.0 (2 CH); 127.3 (2 CH); 129.4 (CH); 139.9 (CH); 144.2 (C). IR (film): 3060, 1600, 720, 700 cm⁻¹. HRMS calcd for C₂₄H₃₄NO₂ [M + H]⁺ 368.2584, found 368.2589.

(2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyl-2-((R)-4-methyl-2-vinyl-2,5-dihydrofuran-2-yl)octahydro-2H-benzo[e][1,3]oxazine (7b). This compound was obtained from **4b** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 0.15 g, 13%. Colorless oil. [α]_D²⁵ = -20.1 (c = 0.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.82-1.06 (m, 2H); 0.89 (s, 3H); 0.93 (d, *J* = 6.5 Hz, 3H); 1.12 (m, 1H); 1.27 (s, 3H); 1.40-1.76 (m, 5H); 1.59 (d, *J* = 1.1 Hz, 3H); 1.93 (m, 1H); 3.49 (td, *J*₁ = 10.4 Hz, *J*₂ = 3.8 Hz, 1H); 3.88 (d, *J* = 18.4 Hz, 1H); 4.22-4.34 (m, 2H); 4.61 (d, *J* = 18.4 Hz, 1H); 4.73 (s, 1H); 4.94 (dd, *J*₁ = 10.7 Hz, *J*₂ = 1.8 Hz, 1H); 5.03 (dd, *J*₁ = 17.3 Hz, *J*₂ = 1.8 Hz, 1H); 5.36 (m, 1H); 6.13 (dd, *J*₁ = 17.3 Hz, *J*₂ = 10.7 Hz, 1H); 7.11 (m, 1H); 7.17-7.26 (m, 2H); 7.30-7.43 (m, 2H); 4.61 (d, *J* = 18.4 Hz, 1H); 4.73 (s, 1H); 4.94 (dd, *J*₁ = 10.7 Hz, *J*₂ = 1.8 Hz, 1H); 5.03 (dd, *J*₁ = 17.3 Hz, *J*₂ = 1.8 Hz, 1H); 5.36 (m, 1H); 6.13 (dd, *J*₁ = 17.3 Hz, *J*₂ = 10.7 Hz, 1H); 7.11 (m, 1H); 7.17-7.26 (m, 2H); 7.30-7.43 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 12.3 (CH₃); 22.3 (CH₃); 22.6 (CH₃); 25.0 (CH₂); 26.7 (CH₃); 31.5 (CH); 35.2 (CH₂); 41.4 (CH₂); 44.5 (CH); 47.2 (CH₂); 57.9 (C); 77.4 (CH); 77.7 (CH₂); 90.8 (CH); 93.9 (C); 112.5 (CH₂); 124.0 (CH); 125.2 (CH); 127.1 (2 CH); 127.5 (2 CH); 139.4 (C); 144.5 (CH); 158.7 (C). IR (film):

3060, 1450, 720, 695 cm⁻¹. HRMS calcd for C₂₅H₃₆NO₂ [M + H]⁺ 382.2741, found 382.2750.

(2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyl-2-((S)-4-methyl-2-vinyl-2,5-dihydrofuran-2-yl)octahydro-2H-benzo[e][1,3]oxazine (8b). This compound was obtained from **4b** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 0.19 g, 17%. Colorless oil. [α]_D²⁵ = -2.8 (c = 0.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.82-1.05 (m, 2H); 0.89 (s, 3H); 0.92 (d, *J* = 6.5 Hz, 3H); 1.22 (m, 1H); 1.27 (s, 3H); 1.28 (s, 3H); 1.40-1.78 (m, 4H); 1.93 (m, 1H); 3.49 (td, *J*₁ = 10.5 Hz, *J*₂ = 3.9 Hz, 1H); 3.92 (d, *J* = 18.7 Hz, 1H); 4.07 (d, *J* = 12.3 Hz, 1H); 4.31 (d, *J* = 12.3 Hz, 1H); 4.56 (d, *J* = 18.7 Hz, 1H); 4.71 (s, 1H); 4.98 (dd, *J*₁ = 10.6 Hz, *J*₂ = 1.7 Hz, 1H); 5.16 (dd, *J*₁ = 17.3 Hz, *J*₂ = 1.7 Hz, 1H); 5.36 (m, 1H); 6.05 (dd, *J*₁ = 17.2 Hz, *J*₂ = 10.6 Hz, 1H); 7.08 (m, 1H); 7.14-7.24 (m, 2H); 7.26-7.45 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 12.0 (CH₃); 22.3 (CH₃); 22.5 (CH₃); 25.0 (CH₂); 26.3 (CH₃); 31.5 (CH); 35.2 (CH₂); 41.4 (CH₂); 44.6 (CH); 46.6 (CH₂); 58.12 (C); 77.2 (CH₂); 77.9 (CH); 89.9 (CH); 94.5 (C); 112.3 (CH₂); 123.6 (CH); 125.0 (CH); 126.8 (2 CH); 127.3 (2 CH); 135.9 (C); 141.0 (CH); 144.6 (C). IR (film): 3020, 1600, 720, 695 cm⁻¹. HRMS calcd for C₂₅H₃₆NO₂ [M + H]⁺ 382.2741, found 382.2744.

(2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyl-2-((R)-3-methyl-2-(prop-1-en-2-yl)-2,5-dihydrofuran-2-yl)octahydro-2H-benzo[e][1,3]oxazine (7c). This compound was obtained from **4c** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ethyl acetate 45:1). Yield: 1.03 g, 92%. White solid. Mp 160-162 °C (from hexane). [α]_D²⁵ = -64.2 (c = 1, CHCl₃). ¹H NMR (300 MHz, CDCl₃): δ 0.83-1.01 (m, 2H); 0.84 (s, 3H); 0.92 (d, *J* = 6.5 Hz, 3H); 1.13 (m, 1H); 1.29 (s, 3H); 1.39-1.70 (m, 4H); 1.72 (s, 3H); 1.79 (d, *J* = 1.7 Hz, 3H); 1.86 (m, 1H); 3.46 (td, *J*₁ = 10.5 Hz, *J*₂ = 4.0 Hz, 1H); 3.84 (d, *J* = 17.7 Hz, 1H); 4.44 (m, 1H); 4.57 (m, 1H); 4.82 (d, *J* = 1.7 Hz, 1H); 4.98 (d, *J* = 17.7 Hz, 1H); 4.99 (d, *J* = 1.7 Hz, 1H); 5.06 (s, 1H); 5.48 (m, 1H); 7.08 (m, 1H); 7.17-7.25 (m, 2H); 7.35-7.37 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 13.0 (CH₃); 20.0 (CH₃); 22.2 (2 CH₃); 24.9 (CH₂); 27.2 (CH₃); 31.5 (CH); 35.1 (CH₂); 41.3 (CH₂); 43.9 (CH); 47.6 (CH₂); 58.4 (C); 74.5 (CH₂); 77.9 (CH); 85.9 (CH); 96.0 (C); 111.7 (CH₂); 121.3 (CH); 124.9 (CH); 127.1 (2 CH); 127.3 (2 CH); 138.9 (C); 145.0 (C); 145.5 (C). IR (Nujol dispersion): 3060, 1640, 720, 695 cm⁻¹. HRMS calcd for C₂₆H₃₈NO₂ [M + H]⁺ 396.2897, found 396.2906.

(2S,4aS,7R,8aR)-3-benzyl-2-((R)-3,4-dimethyl-2-(prop-1-en-2-yl)-2,5-dihydrofuran-2-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (7d). This compound was obtained from **4d** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 0.82 g, 73%. Colorless oil. [α]_D²⁵ = -74.7 (c = 1, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.83 (s, 3H); 0.84-1.06 (m, 2H); 0.92 (d, *J* = 6.5 Hz, 3H); 1.14 (m, 1H); 1.28 (s, 3H); 1.39-1.72 (m, 4H); 1.56 (s, 3H); 1.66 (d, *J* = 1.0 Hz, 3H); 1.71 (s, 3H); 1.84 (m, 1H); 3.43 (td, *J*₁ = 10.5 Hz, *J*₂ = 4.0 Hz, 1H); 3.86 (d, *J* = 17.5 Hz, 1H); 4.32-4.45 (m, 2H); 4.78 (m, 1H); 4.92 (d, 1H, *J* = 17.5 Hz); 4.95 (s, 1H); 5.03 (s, 1H); 7.07 (m, 1H); 7.16-7.21 (m, 2H); 7.35-7.37 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 10.1 (CH₃); 10.5 (CH₃); 20.1 (CH₃); 22.1 (CH₃); 22.3 (CH₃); 25.0 (CH₂); 27.2 (CH₃); 31.5 (CH); 35.2 (CH₂); 41.4 (CH₂); 44.1 (CH); 47.8 (CH₂); 58.5 (C); 77.8 (CH); 78.4 (CH₂); 86.4 (CH); 97.4 (C); 111.2 (CH₂); 124.9 (CH); 127.1 (2 CH); 127.2 (2 CH); 128.2 (C); 129.9 (C); 145.5 (C); 145.6 (C). IR (film): 3020, 1600, 720, 695 cm⁻¹. HRMS calcd for C₂₇H₄₀NO₂ [M + H]⁺ 410.3054, found 410.3058.

(2S,4aS,7R,8aR)-3-benzyl-2-((S)-3,4-dimethyl-2-(prop-1-en-2-yl)-2,5-dihydrofuran-2-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (8d). This compound was obtained from **4d** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 0.15 g, 13%. White solid. Mp 128-130 °C (from hexane). [α]_D²⁵ = +64.3 (c = 1.5, CHCl₃). ¹H

NMR (300 MHz, CDCl₃): δ 0.83-1.03 (m, 2H); 0.89 (s, 3H); 0.90 (d, *J* = 6.6 Hz, 3H); 0.92 (s, 3H); 1.21 (m, 1H); 1.34 (s, 3H); 1.42-1.74 (m, 4H); 1.65 (s, 3H); 1.67 (s, 3H); 1.93 (m, 1H); 3.50 (td, *J*₁ = 10.5 Hz, *J*₂ = 3.9 Hz, 1H); 3.86 (d, *J* = 19.0 Hz, 1H); 3.91 (m, 1H); 4.26 (m, 1H); 4.77 (d, *J* = 19.0 Hz, 1H); 4.89-4.90 (m, 2H); 5.14 (s, 1H); 7.05 (m, 1H); 7.15-7.21 (m, 2H); 7.25-7.27 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 9.3 (CH₃); 10.3 (CH₃); 19.7 (CH₃); 22.2 (CH₃); 22.7 (CH₃); 25.0 (CH₂); 26.2 (CH₃); 31.5 (CH); 35.2 (CH₂); 41.4 (CH₂); 43.8 (CH); 46.2 (CH₂); 58.5 (C); 78.1 (CH); 78.3 (CH₂); 86.2 (CH); 97.4 (C); 109.6 (CH₂); 124.8 (CH); 126.1 (2 CH); 127.2 (2 CH); 128.6 (C); 128.8 (C); 145.2 (C); 148.5 (C). IR (Nujol dispersion): 3085, 1600, 720, 695 cm⁻¹. HRMS calcd for C₂₇H₄₀NO₂ [M + H]⁺ 410.3054, found 410.3062.

(2S,4aS,7R,8aR)-2-((R)-2-allyl-3,6-dihydro-2H-pyran-2-yl)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (7e). This compound was obtained from **4e** (1.2 g) and catalyst **5**, and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 0.67 g, 60%. Colorless oil. [α]_D²⁵ = +27.1 (c = 2.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.87-1.04 (m, 2H); 0.92 (d, *J* = 6.4 Hz, 3H); 0.93 (s, 3H); 1.24 (m, 1H); 1.29 (s, 3H); 1.47 (m, 1H); 1.55-1.78 (m, 3H); 1.81-2.01 (m, 2H); 2.25 (m, 1H); 2.40 (m, 1H); 2.55 (m, 1H); 3.46 (td, *J*₁ = 10.6 Hz, *J*₂ = 3.8 Hz, 1H); 3.86-3.99 (m, 2H); 4.12 (m, 1H); 4.38 (s, 1H); 5.02-5.08 (m, 3H); 5.62 (m, 1H); 5.70 (m, 1H); 6.12 (m, 1H); 7.13 (m, 1H); 7.24-7.29 (m, 2H); 7.40-7.43 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 22.3 (2 CH₃); 25.0 (CH₂); 27.0 (CH₃); 28.5 (CH₂); 31.6 (CH); 35.2 (CH₂); 35.4 (CH₂); 41.5 (CH₂); 44.1 (CH); 47.9 (CH₂); 58.6 (C); 60.7 (CH₂); 76.4 (C); 78.3 (CH); 89.4 (CH); 118.0 (CH₂); 123.1 (CH); 124.9 (CH); 125.2 (CH); 126.8 (2 CH); 127.8 (2 CH); 134.9 (CH); 145.2 (C). IR (film): 3060, 1740, 1640, 730, 670 cm⁻¹. HRMS calcd for C₂₆H₃₈NO₂ [M + H]⁺ 396.2897, found 396.2893.

(2S,4aS,7R,8aR)-2-((S)-2-allyl-3,6-dihydro-2H-pyran-2-yl)-3-benzyl-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (8e). This compound was obtained from **4e** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ethyl acetate 60:1). Yield: 0.71 g, 63%. White solid. Mp 76-78 °C (from pentane). [α]_D²⁵ = -18.7 (c = 1.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.89-1.06 (m, 2H); 94 (d, *J* = 6.5 Hz, 3H); 0.99 (s, 3H); 1.23 (m, 1H); 1.27 (s, 3H); 1.40-1.75 (m, 5H); 1.95 (m, 1H); 2.39 (dd, *J*₁ = 13.4 Hz, *J*₂ = 6.9 Hz, 1H); 2.51 (dd, *J*₁ = 17.4 Hz, *J*₂ = 7.6 Hz, 1H); 2.70 (m, 1H); 3.49 (td, *J*₁ = 10.8 Hz, *J*₂ = 3.8 Hz, 1H); 3.89 (d, *J* = 18.1 Hz, 1H); 3.95 (m, 1H); 4.09 (m, 1H); 4.55 (s, 1H); 4.68 (d, *J* = 18.1 Hz, 1H); 5.12 (m, 2H); 5.48 (m, 1H); 5.55 (m, 1H); 5.89 (m, 1H); 7.14 (m, 1H); 7.20-7.29 (m, 2H); 7.31-7.42 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 22.3 (CH₃); 23.0 (CH₃); 25.0 (CH₂); 27.0 (CH₃); 27.4 (CH₂); 31.5 (CH); 35.2 (CH₂); 37.0 (CH₂); 41.4 (CH₂); 44.5 (CH); 47.5 (CH₂); 58.8 (C); 60.5 (CH₂); 76.6 (C); 78.0 (CH); 88.9 (CH); 117.8 (CH₂); 122.2 (CH); 124.4 (CH); 125.1 (CH); 127.0 (2 CH); 127.6 (2 CH); 134.6 (CH); 144.6 (C). IR (film): 3060, 1640, 720, 670 cm⁻¹. HRMS calcd for C₂₆H₃₈NO₂ [M + H]⁺ 396.2897, found 396.2895.

(2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyl-2-((R)-4-methyl-2-(2-methylallyl)-3,6-dihydro-2H-pyran-2-yl)octahydro-2H-benzo[e][1,3]oxazine (7f). This compound was obtained from **4f** (1.2 g) and catalyst **5**, and purified by flash chromatography (hexanes/ethyl acetate 50:1). Yield: 0.82 g, 73%. Colorless oil. [α]_D²⁵ = +21.6 (c = 1.8, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.78-0.96 (m, 2H); 0.85 (d, *J* = 6.5 Hz, 3H); 0.91 (s, 3H); 1.08 (m, 1H); 1.16 (s, 3H); 1.28-1.65 (m, 5H); 1.52 (s, 3H); 1.70 (s, 3H); 1.82 (m, 1H); 2.16 (d, *J* = 13.7 Hz, 1H); 2.29 (d, *J* = 13.7 Hz, 1H); 2.45 (m, 1H); 3.38 (td, *J*₁ = 10.4 Hz, *J*₂ = 3.9 Hz, 1H); 3.81-3.91 (m, 2H); 4.00 (m, 1H); 4.50 (s, 1H); 4.64 (m, 1H); 4.78-4.80 (m, 2H); 5.14 (m, 1H); 7.05 (m, 1H); 7.14-7.23 (m, 2H); 7.27-7.43 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 20.7 (CH₃); 22.2 (CH₃); 23.0 (CH₃); 24.7 (CH₃); 25.2 (CH₂); 27.2 (CH₃); 31.5 (CH); 34.0 (CH₂); 35.2 (CH₂); 39.4 (CH₂); 41.6 (CH₂); 46.0 (CH); 48.0 (CH₂); 58.9 (C); 60.8 (CH₂); 77.2 (C); 77.3 (CH); 89.7 (CH);

114.4 (CH₂); 117.8 (CH); 125.1 (CH); 127.2 (2 CH); 127.5 (2 CH); 130.7 (C); 142.9 (C); 145.0 (C). IR (film): 3060, 1640, 730, 700 cm⁻¹. HRMS calcd for C₂₈H₄₂NO₂ [M + H]⁺ 424.3210, found 424.3207.

(2S,4aS,7R,8aR)-3-benzyl-4,4,7-trimethyl-2-((S)-4-methyl-2-(2-methylallyl)-3,6-dihydro-2H-pyran-2-yl)octahydro-2H-benzo[e][1,3]oxazine (8f). This compound was obtained from **4f** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 50:1). Yield: 0.66 g, 59%. White solid. Mp 93-95 °C (from hexane). [α]_D²⁵ = -52.0 (c = 2.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.83-1.02 (m, 2H); 0.93 (d, J = 6.4 Hz, 3H); 0.98 (s, 3H); 1.23 (m, 1H); 1.25 (s, 3H); 1.41-1.74 (m, 5H); 1.52 (s, 3H); 1.78 (s, 3H); 1.90 (m, 1H); 2.31 (d, 1H, J = 13.2 Hz); 2.55 (d, 1H, J = 13.2 Hz); 2.62 (m, 1H); 3.48 (td, J₁ = 10.6 Hz, J₂ = 3.9 Hz, 1H); 3.89 (d, J = 17.9 Hz, 1H); 3.94 (m, 1H); 4.06 (m, 1H); 4.62 (s, 1H); 4.78 (d, J = 0.9 Hz, 1H); 4.84 (d, J = 17.9 Hz, 1H); 4.87 (d, J = 0.9 Hz, 1H); 5.23 (m, 1H); 7.11 (m, 1H); 7.19-7.28 (m, 2H); 7.31-7.42 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): 22.2 (CH₃); 22.9 (CH₃); 23.0 (CH₃); 24.5 (CH₃); 25.2 (CH₂); 27.2 (CH₃); 31.7 (CH); 32.8 (CH₂); 35.4 (CH₂); 40.1 (CH₂); 41.6 (CH₂); 44.9 (CH); 47.7 (CH₂); 58.9 (C); 60.9 (CH₂); 77.6 (C); 77.7 (CH); 88.2 (CH); 114.6 (CH₂); 117.9 (CH); 125.1 (CH); 127.2 (2 CH); 127.5 (2 CH); 129.7 (C); 143.0 (C); 144.9 (C). IR (nujol dispersion): 3060, 1640, 730, 700 cm⁻¹. HRMS calcd for C₂₈H₄₂NO₂ [M + H]⁺ 424.3210, found 424.3210.

(2S,4aS,7R,8aR)-3-benzyl-2-((R)-4,5-dimethyl-2-(2-methylallyl)-3,6-dihydro-2H-pyran-2-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (7g). This compound was obtained from **4g** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 60:1). Yield: 0.68 g, 60%. Colorless oil. [α]_D²⁵ = +17.0 (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.84-1.05 (m, 2H); 0.93 (d, J = 6.5 Hz, 3H); 0.99 (s, 3H); 1.20 (m, 1H); 1.23 (s, 3H); 1.35-1.73 (m, 5H); 1.40 (s, 3H); 1.54 (s, 3H); 1.76 (s, 3H); 1.94 (m, 1H); 2.22 (d, J = 13.8 Hz, 1H); 2.35 (d, J = 13.8 Hz, 1H); 2.52 (m, 1H); 3.45 (td, J₁ = 10.4 Hz, J₂ = 4.1 Hz, 1H); 3.76 (m, 1H); 3.86 (m, 1); 3.94 (d, J = 17.8 Hz, 1H); 4.55 (s, 1H); 4.74 (d, J = 17.8 Hz, 1H); 4.84 (s, 2H); 7.12 (m, 1H); 7.17-7.28 (m, 2H); 7.38-7.44 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 13.5 (CH₃); 18.4 (CH₃); 20.8 (CH₃); 22.2 (CH₃); 24.7 (CH₃); 25.2 (CH₂); 27.3 (CH₃); 31.6 (CH); 34.9 (CH₂); 35.3 (CH₂); 39.5 (CH₂); 41.7 (CH₂); 46.0 (CH); 48.1 (CH₂); 58.9 (C); 64.7 (CH₂); 77.3 (CH); 77.8 (C); 89.6 (CH); 114.3 (CH₂); 122.2 (C); 122.7 (C); 125.1 (CH); 127.3 (2 CH); 127.5 (2 CH); 143.1 (C); 145.1 (C). IR (film): 3065, 1635, 735, 700 cm⁻¹. HRMS calcd for C₂₉H₄₄NO₂ [M + H]⁺ 438.3367, found 438.3369.

(2S,4aS,7R,8aR)-3-benzyl-2-((S)-4,5-dimethyl-2-(2-methylallyl)-3,6-dihydro-2H-pyran-2-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (8g). This compound was obtained from **4g** (1.2 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 60:1). Yield: 0.25 g, 22%. White solid. Mp 87-89 °C (from pentane). [α]_D²⁵ = -61.5 (c = 2.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.88-1.03 (m, 2H); 0.93 (d, J = 6.5 Hz, 3H); 0.95 (s, 3H); 1.25 (s, 3H); 1.35 (s, 3H); 1.43-1.72 (m, 5H); 1.47 (s, 3H); 1.77 (s, 3H); 1.90 (m, 1H); 2.28 (d, J = 13.2 Hz, 1H); 2.53 (d, J = 13.2 Hz, 1H); 2.59 (m, 1H); 3.47 (td, J₁ = 10.5 Hz, J₂ = 3.9 Hz, 1H); 3.73 (m, 1H); 3.89 (d, J = 17.9 Hz, 1H); 3.90 (m, 1H); 4.63 (s, 1H); 4.77 (m, 1H); 4.82 (d, J = 17.9 Hz, 1H); 4.88 (m, 1H); 7.09 (m, 1H); 7.20-7.25 (m, 2H); 7.26-7.39 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 13.5 (CH₃); 18.4 (CH₃); 20.8 (CH₃); 22.2 (CH₃); 24.7 (CH₃); 25.2 (CH₂); 27.3 (CH₃); 31.6 (CH); 34.9 (CH₂); 35.3 (CH₂); 39.5 (CH₂); 41.7 (CH₂); 46.0 (CH); 48.1 (CH₂); 58.9 (C); 64.7 (CH₂); 77.3 (CH); 77.8 (C); 89.6 (CH); 114.3 (CH₂); 122.2 (C); 122.7 (C); 125.1 (CH); 127.3 (2 CH); 127.5 (2 CH); 143.1 (C); 145.1 (C). IR (film): 3060, 1635, 725, 695 cm⁻¹. HRMS calcd for C₂₉H₄₄NO₂ [M + H]⁺ 438.3367, found 438.3368.

(2S,4aS,7R,8aR)-3-benzyl-2-((R)-2-ethyl-2,5-dihydrofuran-2-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (14). This compound was obtained from **13** (2.0 g) and catalyst **5**, and purified by flash chromatography (hexanes/ ethyl acetate 45:1). Yield: 1.63 g, 88 %. Colorless oil. [α]_D²⁵ = +6.2 (c = 0.8, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.82 (t, J = 7.4 Hz, 3H); 0.84-1.00 (m, 2H); 0.87 (s, 3H); 0.92 (d, J = 6.5 Hz, 3H); 1.13 (m, 1H); 1.28 (s, 3H); 1.35-1.58 (m, 2H); 1.60-1.73 (m, 4H); 1.86 (m, 1H); 3.44 (td, J₁ = 10.6 Hz, J₂ = 3.9 Hz, 1H); 3.93 (d, J = 18.4 Hz, 1H); 4.48-4.51 (m, 2H); 4.66 (s, 1H); 4.78 (d, J = 18.4 Hz, 1H); 5.65 (m, 1H); 5.84 (m, 1H); 7.11 (m, 1H); 7.22-7.27 (m, 2H); 7.41-7.43 (m, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 8.27 (CH₃); 22.3 (CH₃); 22.7 (CH₃); 24.9 (CH₂); 26.8 (CH₃); 29.7 (CH₂); 31.5 (CH); 35.2 (CH₂); 41.3 (CH₂); 43.8 (CH); 47.3 (CH₂); 57.9 (C); 76.6 (CH₂); 77.6 (CH); 89.9 (CH); 94.5 (C); 125.2 (CH); 126.7 (2 CH); 127.1 (CH); 127.6 (2 CH); 130.7 (CH); 144.9 (C). IR (film): 3058, 1605, 722, 695 cm⁻¹. HRMS calcd for C₂₄H₃₆NO₂ [M + H]⁺ 370.2741, found 370.2750.

(3R,4aR,5aS,6R,11aS)-3,11,11-trimethyl-6-vinyl-2,3,4,4a,5a,6,11,11a-octahydro-1H,9H-benzo[e]pyrido[2,1-b][1,3]oxazin-6-ol (22a). This compound was obtained from **19a** (1.0 g) and catalyst **5**, and purified by flash chromatography (hexanes/ ethyl acetate 20:1). Yield: 0.17 g, 19 %. White solid. Mp 136-138 °C (from hexane). [α]_D²⁵ = -112.2 (c = 1.2, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.90 (d, J = 6.4 Hz, 3H); 0.92-1.25 (m, 3H); 1.18 (s, 3H); 1.22 (s, 3H); 1.46 (m, 1H); 1.56-1.63 (m, 2H); 1.71 (m, 1H); 1.89 (m, 1H); 2.70 (broad, 1H); 3.26 (m, 1H); 3.40 (td, J₁ = 10.7 Hz, J₂ = 3.9 Hz, 1H); 3.48 (m, 1H); 4.52 (s, 1H); 5.20 (dd, J₁ = 10.7 Hz, J₂ = 1.7 Hz, 1H); 5.46 (dd, J₁ = 17.3 Hz, J₂ = 1.7 Hz, 1H); 5.69 (d, J = 9.9 Hz, 1H); 5.89 (ddd, J₁ = 9.9 Hz, J₂ = 4.2 Hz, J₃ = 2.5 Hz, 1H); 6.06 (dd, J₁ = 17.3 Hz, J₂ = 10.7 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 21.0 (CH₃); 22.0 (CH₃); 24.8 (CH₂); 25.8 (CH₃); 31.2 (CH); 34.8 (CH₂); 40.8 (CH₂); 41.3 (CH₂); 43.4 (CH); 56.0 (C); 69.7 (C); 76.7 (CH); 87.7 (CH); 113.4 (CH₂); 126.6 (CH); 127.7 (CH); 139.2 (CH). IR (nujol dispersion): 3320 (broad), 3095, 1655, 830, 730 cm⁻¹. HRMS calcd for C₁₇H₂₈NO₂ [M + H]⁺ 278.2115, found 278.2118.

(3R,4aR,5aS,6S,11aS)-3,11,11-trimethyl-6-vinyl-2,3,4,4a,5a,6,11,11a-octahydro-1H,9H-benzo[e]pyrido[2,1-b][1,3]oxazin-6-ol (23a). This compound was obtained from **19a** (1.0 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 20:1). Yield: 0.24 g, 26 %. Colorless oil. [α]_D²⁵ = -113.3 (c = 1.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.90-1.15 (m, 3H); 0.92 (d, J = 6.6 Hz, 3H); 1.16 (s, 3H); 1.17 (s, 3H); 1.56 (m, 1H); 1.57-1.73 (m, 3H); 1.90 (m, 1H); 3.22 (m, 1H); 3.28 (s, 1H); 3.40 (m, 1H); 3.50 (td, J₁ = 10.3 Hz, J₂ = 3.7 Hz, 1H); 4.55 (s, 1H); 5.13 (dd, J₁ = 10.6 Hz, J₂ = 1.7 Hz, 1H); 5.36 (dd, J₁ = 17.3 Hz, J₂ = 1.7 Hz, 1H); 5.52 (d, J = 10.0 Hz, 1H); 5.78 (m, 1H); 5.93 (dd, J₁ = 17.3 Hz, J₂ = 10.6 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 20.9 (CH₃); 22.0 (CH₃); 24.6 (CH₂); 25.7 (CH₃); 31.1 (CH); 34.7 (CH₂); 40.8 (CH₂); 41.3 (CH₂); 43.1 (CH); 56.0 (C); 70.9 (C); 76.7 (CH); 85.7 (CH); 113.5 (CH₂); 124.8 (HC); 127.1 (HC); 140.7 (HC). IR (film): 3545 (broad), 3040, 725 cm⁻¹. HRMS calcd for C₁₇H₂₈NO₂ [M + H]⁺ 278.2115, found 278.2113.

(3R,4aR,5aS,6R,11aS)-6-methoxy-3,11,11-trimethyl-6-vinyl-2,3,4,4a,5a,6,11,11a-octahydro-1H,9H-benzo[e]pyrido[2,1-b][1,3]oxazine (24a). This compound was obtained from **20a** (1.0 g) and catalyst **5**, and purified by flash chromatography (hexanes/ ethyl acetate 20:1). Yield: 0.55 g, 60%. Colorless oil. [α]_D²⁵ = -132.3 (c = 0.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.89 (d, J = 6.5 Hz, 3H); 0.95-1.01 (m, 2H); 1.05 (m, 1H); 1.21 (s, 3H); 1.26 (s, 3H); 1.42-1.60 (m, 3H); 1.69 (m, 1H); 1.84 (m, 1H); 3.24 (s, 3H); 3.33-3.53 (m, 3H); 4.65 (s, 1H); 5.28 (dd, J₁ = 10.8 Hz, J₂ = 1.2 Hz, 1H); 5.30 (dd, J₁ = 17.8 Hz, J₂ = 1.2 Hz, 1H); 5.82 (m, 1H); 5.83 (dd, J₁ = 17.8 Hz, J₂ = 10.8 Hz, 1H); 6.10 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 21.0 (CH₃); 22.1 (CH₃); 25.0 (CH₂); 26.0 (CH₃); 31.4 (CH); 35.0 (CH₂); 41.1 (CH₂); 41.9 (N-CH₂); 43.5 (CH); 50.8

(CH₃); 56.0 (C); 75.1 (C); 76.9 (CH); 86.7 (CH); 115.5 (CH₂); 121.5 (HC); 131.0 (HC); 138.7 (HC). IR (film): 3085, 1650, 81, 730 cm⁻¹. HRMS calcd for C₁₈H₃₀NO₂ [M + H]⁺ 292.2271, found 292.2273

(3R,4aR,5aS,6S,11aS)-6-methoxy-3,11,11-trimethyl-6-vinyl-2,3,4,4a,5a,6,11,11a-octahydro-1H,9H-benzo[e]pyrido[2,1-b][1,3]oxazine (25a). This compound was obtained from **20a** (1.0 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 20:1). Yield: 0.58 g, 64%. White solid. Mp 77-79 °C (from pentane). [α]_D²⁵ = -129.9 (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.86-1.02 (m, 2H); 0.91 (d, *J* = 6.5 Hz, 3H); 1.13 (m, 1H); 1.15 (s, 3H); 1.20 (s, 3H); 1.50 (m, 1H); 1.54-1.72 (m, 2H); 1.98 (m, 1H); 3.22 (m, 1H); 3.32 (s, 3H); 3.43-3.51 (m, 2H); 4.75 (s, 1H); 5.23 (dd, *J*₁ = 10.7 Hz, *J*₂ = 1.4 Hz, 1H), 5.28 (dd, *J*₁ = 17.7 Hz, *J*₂ = 1.4 Hz, 1H); 5.60 (d, *J* = 10.2 Hz, 1H); 5.81 (m, 1H); 5.85 (dd, *J*₁ = 17.7 Hz, *J*₂ = 10.7 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 21.5 (CH₃); 22.2 (CH₃); 25.0 (CH₂); 26.1 (CH₃); 31.5 (CH); 35.0 (CH₂); 41.3 (CH₂); 41.9 (CH₂); 43.1 (CH); 50.6 (CH₃); 56.3 (C); 76.5 (C) 77.1 (CH); 84.5 (CH); 115.8 (CH₂); 124.0 (CH); 126.1 (CH); 139.7 (CH). IR (film): 3085, 1664, 723, 656 cm⁻¹. HRMS calcd for C₁₈H₃₀NO₂ [M + H]⁺ 292.2271, found 292.2271

(3R,4aR,5aS,6R,11aS)-6-methoxy-3,7,11,11-tetramethyl-6-(prop-1-en-2-yl)-2,3,4,4a,5a,6,11,11a-octahydro-1H,9H-benzo[e]pyrido[2,1-b][1,3]oxazine (24b). This compound was obtained from **20b** (1.0 g) and catalyst **6**, and purified by flash chromatography in CH₂Cl₂. Yield: 0.69 g, 75%. Colorless oil. [α]_D²⁵ = -76.4 (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.89 (d, *J* = 6.5 Hz, 3H); 0.91-1.13 (m, 3H); 1.12 (s, 3H); 1.14 (s, 3H); 1.19-1.47 (m, 2H); 1.55 (d, *J* = 1.5 Hz, 3H); 1.56-1.75 (m, 2H); 1.76 (s, 3H); 1.89 (m, 1H); 3.16 (m, 1H); 3.30 (s, 3H); 3.36 (td, *J*₁ = 10.4 Hz, *J*₂ = 4.0 Hz, 1H); 3.45 (m, 1H); 4.59 (s, 1H); 4.93 (d, *J* = 1.2 Hz, 1H); 5.15 (m, 1H, CHH=); 5.87 (d, *J* = 1.2 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 17.8 (CH₃); 18.4 (CH₃); 20.9 (CH₃); 22.1 (CH₃); 24.8 (CH₂); 26.4 (CH₃); 31.1 (CH); 34.8 (CH₂); 40.9 (2CH₂); 44.9 (CH); 51.9 (CH₃); 55.5 (C); 75.6 (CH); 81.7 (C); 87.4 (CH); 111.6 (CH₂); 127.1 (CH); 139.2 (C); 145.9 (C). IR (film): 3085, 1675, 810, 735, 645 cm⁻¹. HRMS calcd for C₂₀H₃₄NO₂ [M + H]⁺ 320.2584, found 320.2587

(3R,4aR,5aS,6R,12aS)-3,8,12,12-tetramethyl-6-(2-methylallyl)-2,3,4,4a,5a,6,7,10,12,12a-decahydro-1H-benzo[5,6][1,3]oxazino[3,2-a]azepin-6-ol (22c). This compound was obtained from **19c** (1.0 g) and catalyst **5**, and purified by flash chromatography (hexanes/ ethyl acetate 35:1). Yield: 0.66 g, 72%. Colorless oil. [α]_D²⁵ = -38.1 (c = 1.0, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 0.84-0.93 (m, 2H); 0.92 (d, *J* = 6.5 Hz, 3H); 1.09 (m, 1H); 1.14 (s, 3H); 1.16 (s, 3H); 1.38 (m, 1H); 1.43 (m, 1H); 1.51 (m, 1H); 1.66 (m, 1H); 1.70 (s, 3H); 1.76 (m, 1H); 1.85 (s, 3H); 2.14 (d, *J* = 13.5 Hz, 1H); 2.35 (d, *J* = 13.5 Hz, 1H); 2.78-2.91 (m, 3H); 3.36 (td, *J*₁ = 10.7 Hz, *J*₂ = 3.9 Hz, 1H); 3.62 (dd, *J*₁ = 13.5 Hz, *J*₂ = 6.4 Hz, 1H); 4.48 (s, 1H); 4.74 (m, 1H); 4.89 (m, 1H); 5.64 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 22.2 (2 CH₃); 24.5 (CH₃); 25.1 (CH₂); 26.2 (CH₃); 28.6 (CH₃); 31.4 (CH); 35.0 (CH₂); 37.4 (CH₂); 39.2 (CH₂); 41.1 (CH₂); 45.8 (CH); 46.9 (CH₂); 57.8 (C); 70.7 (C); 76.7 (CH); 89.4 (CH); 114.4 (CH₂); 124.6 (CH); 139.5 (C); 143.3 (C). δ IR (film): 3080, 1640, 740, 670 cm⁻¹. HRMS calcd for C₂₁H₃₆NO₂ [M + H]⁺ 334.2741, found 334.2741.

(3R,4aR,5aS,6S,12aS)-3,8,12,12-tetramethyl-6-(2-methylallyl)-2,3,4,4a,5a,6,7,10,12,12a-decahydro-1H-benzo[5,6][1,3]oxazino[3,2-a]azepin-6-ol (23c). This compound was obtained from **19c** (1.0 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 35:1). Yield: 0.18 g, 20%. Colorless oil. [α]_D²⁵ = -55.2 (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.84-1.02 (m, 1H); 0.93 (d, *J* = 6.4 Hz, 3H); 1.07 (m, 1H); 1.16 (s, 3H); 1.16 (s, 3H); 1.30 (m, 1H); 1.48 (m, 1H); 1.54 (m, 1H); 1.66 (m, 1H); 1.73 (s, 3H); 1.85 (s, 3H); 1.91 (m, 1H); 2.23 (d, *J* = 15.5 Hz, 1H); 2.25 (d, *J* = 13.5 Hz,

1H); 2.39 (d, *J* = 13.5 Hz, 1H); 2.50 (d, *J* = 15.5 Hz, 1H); 2.98 (dd, *J*₁ = 15.2 Hz, *J*₂ = 7.5 Hz, 1H); 3.07 (s broad, 1H); 3.49 (td, *J*₁ = 10.5 Hz, *J*₂ = 4.0 Hz, 1H); 3.54 (m, 1H); 4.57 (s, 1H); 4.76 (d, *J* = 0.9 Hz, 1H); 4.87 (d, *J* = 0.9 Hz, 1H); 5.50 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 20.7 (CH₃); 22.2 (CH₃); 24.8 (CH₃); 25.0 (CH₂); 26.1 (CH₃); 28.1 (CH₃); 31.3 (CH); 34.9 (CH₂); 39.1 (CH₂); 40.6 (CH₂); 41.1 (CH₂); 46.1 (CH); 47.3 (CH₂); 57.3 (C); 70.4 (C); 76.1 (CH); 89.2 (CH); 114.7 (CH₂); 124.2 (CH); 136.1 (C); 143.0 (C). IR (film): 3545, 3070, 1640, 740, 630 cm⁻¹. HRMS calcd for C₂₁H₃₆NO₂ [M + H]⁺ 334.2741, found 334.2743.

(3R,4aR,5aS,6R,12aS)-6-methoxy-3,8,12,12-tetramethyl-6-(2-methylallyl)-2,3,4,4a,5a,6,7,10,12,12a-decahydro-1H-benzo[5,6][1,3]oxazino[3,2-a]azepine (24c). This compound was obtained from **20c** (1.0 g) and catalyst **5**, and purified by flash chromatography (hexanes/ ethyl acetate 30:1). Yield: 0.87 g, 94%. White solid. Mp 59-61 °C (from pentane) [α]_D²⁵ = -38.9 (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.84-0.99 (m, 2H); 0.91 (d, *J* = 6.5 Hz, 3H); 1.02 (m, 1H); 1.08 (s, 3H); 1.16 (s, 3H); 1.31 (m, 1H); 1.43 (m, 1H); 1.54 (m, 1H); 1.68 (m, 1H); 1.74 (s, 3H); 1.83 (s, 3H); 1.87 (m, 1H); 2.06 (d, *J* = 16.1 Hz, 1H); 2.28 (d, *J* = 14.8 Hz, 1H); 2.42 (d, *J* = 14.8 Hz, 1H); 2.56 (d, *J* = 16.1 Hz, 1H); 3.15 (dd, *J*₁ = 15.6 Hz, *J*₂ = 5.6 Hz, 1H); 3.22 (s, 3H); 3.33 (td, *J*₁ = 10.6 Hz, *J*₂ = 4.0 Hz, 1H); 3.40 (m, 1H); 4.43 (s, 1H); 4.81 (d, *J* = 0.9 Hz, 1H); 4.86 (d, *J* = 0.9 Hz, 1H); 5.49 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 17.7 (CH₃); 21.9 (CH₃); 24.0 (CH₃); 24.8 (CH₂); 25.5 (CH₃); 27.3 (CH₃); 30.8 (CH); 34.6 (CH₂); 37.4 (CH₂); 38.6 (CH₂); 39.2 (CH₂); 40.8 (CH₂); 47.1 (CH); 49.3 (CH₃); 57.0 (C); 75.4 (CH); 80.6 (C); 88.9 (CH); 113.6 (CH₂); 124.6 (CH); 134.1 (C); 142.1 (C). IR (nujol dispersion): 3075, 1640, 1455, 890 cm⁻¹. HRMS calcd for C₂₂H₃₈NO₂ [M + H]⁺ 348.2897, found 348.2906.

(3R,4aR,5aS,6S,12aS)-6-((tert-butyl)dimethylsilyloxy)-3,8,12,12-tetramethyl-6-(2-methylallyl)-2,3,4,4a,5a,6,7,10,12,12a-decahydro-1H-benzo[5,6][1,3]oxazino[3,2-a]azepine (27c). This compound was obtained from **21c** (0.6 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 80:1). Yield: 0.48 g, 85%. Colorless oil [α]_D²⁵ = -81.5 (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.07 (s, 3H); 0.78 (s, 3H); 0.85 (s, 9H); 0.86-0.98 (m, 2H); 0.93 (d, *J* = 6.6 Hz, 3H); 1.11 (m, 1H); 1.13 (s, 3H); 1.15 (s, 3H); 1.35 (m, 1H); 1.42-1.52 (m, 2H); 1.61 (m, 1H); 1.71 (s, 3H); 1.82 (s, 3H); 1.93-2.00 (m, 2H); 2.31 (d, *J* = 13.2 Hz, 1H); 2.46 (d, *J* = 13.2 Hz, 1H); 2.76 (d, *J* = 14.8 Hz, 1H); 2.93 (dd, *J*₁ = 14.5 Hz, *J*₂ = 8.2 Hz, 1H); 3.45 (td, *J*₁ = 10.6 Hz, *J*₂ = 3.9 Hz, 1H); 3.69 (m, 1H); 4.71 (s, 1H); 4.82 (m, 1H); 4.84 (m, 1H); 5.44 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ -2.5 (CH₃); -1.6 (CH₃); 18.8 (C); 22.9 (CH₃); 22.4 (CH₂); 25.2 (CH₂ + CH₃); 26.3 (3 CH₃); 26.4 (CH₂); 28.7 (CH₃); 31.4 (CH); 35.1 (CH₂); 38.3 (CH₂); 41.1 (CH₂); 42.2 (CH₂); 45.4 (CH); 47.1 (CH₂); 57.5 (C); 76.4 (O); 77.8 (C); 88.6 (CH); 115.3 (CH₂); 124.4 (CH); 136.9 (C); 142.7 (C). IR (film): 3075, 1640, 705, 620 cm⁻¹. HRMS calcd for C₂₇H₅₀NO₂Si [M + H]⁺ 448.3605, found 448.3600.

(3R,4aR,5aS,6R,12aS)-6-methoxy-3,12,12-trimethyl-6-vinyl-2,3,4,4a,5a,6,9,10,12,12a-decahydro-1H-benzo[5,6][1,3]oxazino[3,2-a]azepine (24d). This compound was obtained from **20d** (1.0 g) and catalyst **5**, and purified by flash chromatography (hexanes/ ethyl acetate 25:1). Yield: 0.37 g, 40%. Colorless oil. [α]_D²⁵ = -75.2 (c = 1.0, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 0.78-0.93 (m, 2H); 0.85 (d, *J* = 6.6 Hz, 3H); 1.03 (m, 1H); 1.08 (m, 3H); 1.12 (s, 3H); 1.29 (m, 1H); 1.39 (m, 1H); 1.55 (m, 1H); 1.62 (m, 1H); 1.85 (m, 1H); 2.13 (m, 1H); 2.23 (m, 1H); 2.92 (ddd, 1H, *J*₁ = 14.1 Hz, *J*₂ = 7.4 Hz, *J*₃ = 4.2 Hz, 1H); 3.07 (m, 1H); 3.11 (s, 3H); 3.34 (td, *J*₁ = 10.6 Hz, *J*₂ = 4.1 Hz); 4.51 (s, 1H); 5.20 (dd, *J*₁ = 10.7 Hz, *J*₂ = 1.6 Hz, 1H); 5.22 (dd, *J*₁ = 17.5 Hz, *J*₂ = 1.6 Hz, 1H); 5.45 (dt, 1H, *J*₁ = 11.5 Hz, *J*₂ = 1.6 Hz, 1H); 5.94 (m, 1H); 5.95 (dd, *J*₁ = 17.5 Hz, *J*₂ = 10.7 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 18.4 (CH₃); 22.2 (CH₃); 27.2 (CH₃); 31.3 (CH); 32.3 (CH₂); 34.9 (CH₂); 38.3 (CH₂); 41.2 (CH₂); 48.0

(CH); 50.3 (CH); 57.1 (C); 76.5 (CH); 81.2 (C); 92.3 (CH); 114.6 (CH₂); 140.4 (CH). IR (film): 3075, 1740, 1455, 725 cm⁻¹. HRMS calcd for C₁₉H₃₂NO₂ [M + H]⁺ 306.2428, found 306.2428.

(3R,4aR,5aS,6S,12aS)-6-methoxy-3,12,12-trimethyl-6-vinyl-2,3,4,4a,5a,6,9,10,12,12a-decahydro-1H-benzo[5,6][1,3]oxazino[3,2-a]azepine (25d). This compound was obtained from **20d** (1.0 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 25:1). Yield: 0.57 g, 62%. Colorless oil. $[\alpha]_D^{25} = -92.8$ (c = 1.5, CHCl₃). ¹H NMR (300 MHz, CDCl₃): δ 0.81-0.98 (m, 2H); 0.89 (d, J = 6.5 Hz, 3H); 1.09 (m, 1H); 1.16 (s, 3H); 1.23 (s, 3H); 1.40-1.51 (m, 2H); 1.54 (m, 1H); 1.66 (m, 1H); 2.00 (m, 1H); 2.02-2.26 (m, 2H); 2.93 (ddd, J₁ = 13.6 Hz, J₂ = 7.5 Hz, J₃ = 2.7 Hz, 1H); 3.19 (m, 1H); 3.24 (s, 3H); 3.54 (td, J₁ = 10.5 Hz, J₂ = 3.9 Hz, 1H); 4.78 (s, 1H); 5.32 (dd, J₁ = 10.5 Hz, J₂ = 1.7 Hz, 1H); 5.35 (dd, J₁ = 17.5 Hz, J₂ = 1.7 Hz, 1H); 5.66 (d, J = 11.3 Hz, 1H); 5.82 (dd, J₁ = 17.5 Hz, J₂ = 10.5 Hz, 1H); 6.0 (dt, J₁ = 11.3 Hz, J₂ = 5.5 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 22.2 (CH₃); 22.2 (CH₃); 25.4 (CH₂); 28.1 (CH₃); 29.9 (CH₂); 31.3 (CH); 35.0 (CH₂); 40.8 (CH₂); 41.5 (CH₂); 46.9 (CH); 50.8 (CH₃); 57.7 (C); 77.1 (O); 82.1 (C); 90.1 (CH); 116.0 (CH₂); 127.8 (CH); 132.4 (CH); 137.7 (CH). IR (film): 3080, 1660, 730 cm⁻¹. HRMS calcd for C₁₉H₃₂NO₂ [M + H]⁺ 306.2428, found 306.2431.

(3R,4aR,5aS,6S,12aS)-6-((tert-butyl)dimethylsilyloxy)-3,12,12-trimethyl-6-vinyl-2,3,4,4a,5a,6,9,10,12,12a-decahydro-1H-benzo[5,6][1,3]oxazino[3,2-a]azepine (27d). This compound was obtained from **21d** (0.70 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 50:1). Yield: 0.62 g, 94%. White solid. Mp 80-81 °C (from hexane) $[\alpha]_D^{25} = -100.9$ (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.08 (s, 3H); 0.16 (s, 3H); 0.85-1.01 (m, 2H); 0.89 (s, 9H); 0.91 (d, J = 6.6 Hz, 3H); 1.02 (m, 1H); 1.16 (s, 3H); 1.20 (s, 3H); 1.41-1.53 (m, 2H); 1.59 (m, 1H); 1.70 (m, 1H); 1.92 (m, 1H); 2.14 (m, 1H); 2.30 (m, 1H); 2.93 (ddd, J₁ = 13.7 Hz, J₂ = 8.3 Hz, J₃ = 1.9 Hz, 1H); 3.20 (ddd, J₁ = 13.7 Hz, J₂ = 9.1 Hz, J₃ = 1.6 Hz, 1H); 3.46 (td, J₁ = 10.6 Hz, J₂ = 3.8 Hz, 1H); 4.54 (s, 1H); 5.05 (dd, J₁ = 10.5 Hz, J₂ = 1.9 Hz, 1H); 5.42 (d, J = 11.2 Hz, 1H); 5.43 (dd, J₁ = 17.1 Hz, J₂ = 1.9 Hz); 5.72 (dt, J₁ = 11.2 Hz, J₂ = 5.6 Hz, 1H); 6.12 (dd, J₁ = 17.0 Hz, J₂ = 10.5 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ -2.9 (CH₃); -2.5 (CH₃); 18.7 (C); 22.3 (CH₃); 22.8 (CH₃); 25.4 (CH₂); 26.0 (3 CH₃); 28.5 (CH₃); 30.0 (CH₂); 31.4 (CH); 35.2 (CH₂); 41.3 (CH₂); 41.7 (CH₂); 46.8 (CH); 57.8 (C); 77.1 (CH); 80.3 (C); 91.3 (CH); 112.6 (CH₂); 128.9 (CH); 134.9 (CH); 141.2 (CH). IR (nujol dispersion): 3080, 1640, 740, 670 cm⁻¹. HRMS calcd for C₂₄H₄₄NO₂Si [M + H]⁺ 406.3136, found 406.3142.

(3R,4aR,5aS,6R,13aS,Z)-3,8,13,13-tetramethyl-6-(2-methylallyl)-2,3,4,4a,5a,6,10,11,13,13a-decahydro-1H,7H-benzo[5,6][1,3]oxazino[3,2-a]azocin-6-ol (22e) This compound was obtained from **19e** (1.0 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 50:1). Yield: 0.46 g, 50%. Colorless oil $[\alpha]_D^{25} = -5.6$ (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.85-0.98 (m, 2H); 0.91 (d, J = 5.9 Hz, 3H); 1.06 (m, 1H); 1.13 (s, 3H); 1.17 (s, 3H); 1.22-1.33 (m, 2H); 1.44 (m, 1H); 1.57 (m, 1H); 1.67 (m, 1H); 1.77 (s, 3H); 1.87 (s, 3H); 2.05 (m, 1H); 2.18 (d, J = 13.5 Hz, 1H); 2.24 (m, 1H); 2.42 (d, J = 14.5 Hz, 1H); 2.47 (d, J = 14.5 Hz, 1H); 2.61 (d, J = 13.5 Hz, 1H); 2.82 (m, 1H); 3.21 (ddd, J₁ = 16.1 Hz, J₂ = 9.4 Hz, J₃ = 2.1 Hz, 1H); 3.45 (td, J₁ = 10.6 Hz, J₂ = 3.9 Hz, 1H); 4.41 (s, 1H); 4.77 (m, 1H); 4.85 (m, 1H); 5.54 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 22.2 (2 CH₃); 22.7 (CH₃); 25.0 (CH₂); 26.7 (CH₃); 28.9 (CH₃); 31.4 (CH); 33.4 (CH₂); 35.1 (CH₂); 39.1 (CH₂); 40.9 (CH₂); 41.4 (CH₂); 46.0 (CH); 49.8 (CH₂); 57.7 (C); 75.6 (C); 76.9 (CH); 88.7 (CH); 114.8 (CH₂); 126.0 (CH); 133.6 (CH); 143.5 (C). IR (film): 3320 (broad), 3090, 1650, 705 cm⁻¹. HRMS calcd for C₂₂H₃₈NO₂ [M + H]⁺ 348.2897, found 348.2899.

(3R,4aR,5aS,6R,13aS,Z)-6-methoxy-3,8,13,13-tetramethyl-6-(2-methylallyl)-

2,3,4,4a,5a,6,10,11,13,13a-decahydro-1H,7H-benzo[5,6][1,3]oxazino[3,2-a]azocine (24e). This compound was obtained from **20e** (1.0 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 25:1). Yield: 0.82 g, 88%. Colorless oil $[\alpha]_D^{25} = -27.7$ (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.80-0.97 (m, 2H); 0.90 (d, J = 6.6 Hz, 3H); 1.01 (m, 1H); 1.17 (s, 6H); 1.28 (m, 1H); 1.42 (m, 1H); 1.56 (m, 1H); 1.67 (m, 1H); 1.78 (d, J = 1.5 Hz, 3H); 1.80 (m, 1H); 1.84 (s, 3H); 2.03 (d, J = 16.1 Hz, 1H); 2.15-2.21 (m, 2H); 2.36 (d, J = 15.1 Hz, 1H); 2.45 (d, J = 15.1 Hz, 1H); 2.87 (m, 1H); 3.00 (dt, J₁ = 16.3 Hz, J₂ = 5.3 Hz, 1H); 3.21 (dt, J₁ = 16.3 Hz, J₂ = 6.2 Hz, 1H); 3.27 (s, 3H); 3.37 (td, J₁ = 10.6 Hz, J₂ = 3.9 Hz, 1H); 4.61 (s, 1H); 4.83 (m, 1H); 4.89 (m, 1H); 5.40 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 20.8 (CH₃); 22.3 (CH₃); 24.0 (CH₃); 25.1 (CH₂); 27.1 (CH₃); 29.6 (CH₃); 31.4 (CH); 32.8 (CH₂); 35.1 (CH₂); 37.5 (CH₂); 39.3 (CH₂); 41.4 (CH₂); 42.1 (CH₂); 47.1 (CH); 50.5 (CH₃); 58.1 (C); 76.1 (CH); 81.1 (C); 86.9 (CH); 114.0 (CH₂); 124.8 (CH); 130.5 (C); 143.2 (C). IR (film): 3075, 1640, 735, 630 cm⁻¹. HRMS calcd for C₂₃H₄₀NO₂ [M + H]⁺ 362.3054, found 362.3063.

(3R,4aR,5aS,6S,13aS,Z)-6-methoxy-3,8,13,13-tetramethyl-6-(2-methylallyl)-2,3,4,4a,5a,6,10,11,13,13a-decahydro-1H,7H-benzo[5,6][1,3]oxazino[3,2-a]azocine (25e). This compound was obtained from **20e** (1.0 g) and catalyst **6**, and purified by flash chromatography (hexanes/ ethyl acetate 25:1). Yield: 0.02 g, 2%. Colorless oil $[\alpha]_D^{25} = -28.4$ (c = 0.3, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ (m, 1H); 0.82-0.97 (m, 2H); 0.90 (d, J = 6.5 Hz, 3H); 1.08 (m, 1H); 1.12 (s, 3H); 1.14 (s, 3H); 1.27 (m, 1H); 1.46 (m, 1H); 1.54 (m, 1H); 1.66 (m, 1H); 1.77 (d, J = 1.5 Hz, 3H); 1.82 (s, 3H); 1.88 (m, 1H); 2.05-2.15 (m, 2H); 2.30 (d, J = 15.0 Hz, 1H); 2.37 (d, 1H, CHH-C=, J = 15.4 Hz); 2.52 (d, 1H, CHH-C=, J = 15.0 Hz); 2.58 (d, J = 15.4 Hz, 1H); 2.85 (dt, J₁ = 15.9 Hz, J₂ = 4.1 Hz, 1H); 3.31 (td, J₁ = 10.5 Hz, J₂ = 3.9 Hz, 1H); 3.35 (s, 3H); 3.75 (ddd, J₁ = 15.9 Hz, J₂ = 11.0 Hz, J₃ = 10.5 Hz, 1H); 4.47 (s, 1H); 4.86 (s, 2H); 5.44 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): 20.6 (CH₃); 21.2 (CH₃); 24.4 (CH₃); 25.1 (CH₂); 26.4 (CH₃); 29.6 (CH₃); 31.4 (CH); 32.9 (CH₂); 35.1 (CH₂); 38.9 (CH₂); 39.8 (CH₂); 41.5 (CH₂); 42.1 (CH₂); 46.9 (CH); 51.0 (CH₃); 57.4 (C); 76.7 (CH); 81.1 (C); 88.5 (CH); 113.9 (CH₂); 125.9 (CH); 131.3 (C=); 143.3 (C). IR (film): 3069, 1636, 620 cm⁻¹. HRMS calcd for C₂₃H₄₀NO₂ [M + H]⁺ 362.3054, found 362.3057.

General procedure for hydrogenation of compounds **7a**, **7f** and **14**.

A mixture of the unsaturated oxazine (0.15 g) and 10 wt % palladium on carbon (15 mg) in ethanol (1 mL) was stirred at room temperature under H₂ at atmospheric pressure until the reaction was complete (TLC, 16-24 h). The catalyst was separated by filtration over a pad of Celite, after which the solvent was eliminated on a rotavapor, and the residue was purified by flash chromatography on silica gel.

(2S,4aS,7R,8aR)-2-((2R,4R)-2-isobutyl-4-methyltetrahydro-2H-pyran-2-yl)-4,4,7-trimethyloctahydro-2H-benzo[e][1,3]oxazine (9). This compound was obtained from **7f** (0.15 g) and, and purified by flash chromatography (hexanes/ ethyl acetate 12:1). Yield: 55 mg, 46 %. White solid. Mp 65-67 °C (from pentane). $[\alpha]_D^{25} = -15.5$ (c = 0.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.80-0.96 (m, 2H); 0.84 (d, J = 6.5 Hz, 3H); 0.89 (d, J = 6.5 Hz, 3H); 0.90 (d, J = 6.6 Hz, 3H); 0.92 (d, J = 6.6 Hz, 3H); 0.98-1.13 (m, 2H); 1.00 (s, 3H); 1.04 (s, 3H); 1.25 (m, 1H); 1.29 (m, 1H); 1.36-1.52 (m, 4H); 1.59-1.69 (m, 2H); 1.71-1.80 (m, 2H); 1.94 (m, 1H); 2.03 (m, 1H); 3.27 (td, J₁ = 10.4 Hz, J₂ = 4.0 Hz, 1H); 3.66 (m, 1H); 3.91 (m, 1H); 4.39 (s, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 19.7 (CH₃); 22.3 (CH₃); 23.3 (CH₃); 23.6 (CH); 24.8 (CH₃); 25.3 (CH₃); 25.6 (CH); 25.7 (CH₂); 30.1 (CH₃); 31.4 (CH); 24.2 (CH₂); 35.1 (CH₂); 39.6 (CH₂); 42.0 (CH₂); 46.2 (CH₂); 50.8 (C); 52.2 (CH); 62.8 (CH₂); 75.3

(CH); 76.6 (C); 85.1 (CH). HRMS calcd for C₂₁H₄₀NO₂ [M + H]⁺ 338.3054, found 338.3056

(2*S*,4*aS*,7*R*,8*aR*)-2-((*R*)-2-ethyltetrahydrofuran-2-yl)-4,4,7-trimethyloctahydro-2*H*-benzo[*e*][1,3]oxazine (10).

This compound was obtained from **7a** (0.15g) and purified by flash chromatography (hexanes/ ethyl acetate 12:1). Yield: 61 mg, 53 %. Colorless oil. [α]_D²⁵ = -8.4 (c = 0.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 0.76-1.24 (m, 4H); 0.83 (t, *J* = 7.6 Hz, 3H); 0.88 (d, *J* = 6.5 Hz, 3H); 1.00 (s, 3H); 1.03 (s, 3H); 1.42 (m, 1H); 1.50-1.68 (m, 5H); 1.76 (m, 1H); 1.85 (m, 1H); 1.93 (m, 1H); 2.08 (m, 1H); 3.29 (td, *J*₁ = 10.4 Hz, *J*₂ = 4.0 Hz, 1H); 3.74-3.90 (m, 2H); 4.13 (s, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 8.5 (CH₃); 19.7 (CH₃); 22.3 (CH₃); 25.8 (CH₂); 26.6 (CH₂); 29.5 (CH₂); 29.9 (CH₃); 30.8 (CH₂); 31.4 (CH); 35.1 (CH₂); 41.8 (CH₂); 50.7 (C); 51.6 (CH); 69.2 (CH₂); 75.1 (CH); 85.6 (CH); 86.3 (C). HRMS calcd for C₁₇H₃₂NO₂ [M + H]⁺ 282.2428, found 282.2432.

General method for the elimination of the chiral auxiliary in 7a and 7c-g. A mixture of the oxazine **7** (2 mmol), ethanol (20 mL) and a 3% aqueous solution of HCl (20 mL) was heated at reflux until the reaction was finished (TLC and ¹H-NMR were used to monitor the reaction for disappearance of starting material). The mixture was cooled to 0 °C, the pH was adjusted to 7-8 by addition of a 15% solution of NaOH and NaBH₄ (226 mg, 6 mmol) was added. The mixture was further stirred for 3 h at 0 °C. Then 40 mL of H₂O was added and the mixture was stirred for 1 h at room temperature. The aqueous mixture was extracted with ethyl ether (4 x 20 mL). The combined organic layers were washed with brine, dried over MgSO₄, concentrated by distillation at atmospheric pressure and the resulting residue was purified by flash chromatography on silica gel.

(*R*)-(2-vinyl-2,5-dihydrofuran-2-yl)methanol (15a). This compound was obtained from **7a** (0.9 g) and purified by flash chromatography (hexanes/ ethyl ether 15:1). Yield: 0.22 g, 72%. Colorless oil. [α]_D²⁵ = +325.0 (c = 0.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 1.88 (s broad, 1H); 3.62 (m, 2H); 4.71-4.78 (m, 2H); 5.18 (dd, *J*₁ = 10.7 Hz, *J*₂ = 1.5 Hz, 1H); 5.33 (dd, *J*₁ = 17.3 Hz, *J*₂ = 1.5 Hz, 1H); 5.76 (m, 1H); 5.90 (dd, *J*₁ = 17.1 Hz, *J*₂ = 10.7 Hz, 1H); 6.02 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 67.1 (CH₂); 75.4 (CH₂); 93.1 (C); 115.1 (CH₂); 128.2 (CH); 128.8 (CH); 137.6 (CH). IR (film): 3245 (broad), 1640, 1420, 815, 725 cm⁻¹. HRMS calcd for C₇H₁₀NaO₂ [M + Na]⁺ 149.0573, found 149.0578.

(*R*)-(3-methyl-2-(prop-1-en-2-yl)-2,5-dihydrofuran-2-yl)methanol (15c). This compound was obtained from **7c** (1.0 g) and purified by flash chromatography (hexanes/ ethyl ether 15:1). Yield: 0.27 g, 70%. Colorless oil. [α]_D²⁵ = -136.5 (c = 0.6, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 1.66 (m, 3H); 1.71 (m, 3H); 2.08 (s broad, 1H); 3.80 (m, 2H); 4.64 (m, 2H); 4.80 (s, 1H); 4.93 (s, 1H); 5.68 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 11.8 (CH₃); 18.9 (CH₃); 64.2 (CH₂); 75.0 (CH₂); 95.2 (C); 111.1 (CH₂); 122.7 (CH); 136.6 (C); 145.3 (C). IR (film): 3450 (broad), 3090, 1640, 900, 860, 780, 765, 680 cm⁻¹. HRMS calcd for C₉H₁₄NaO₂ [M + Na]⁺ 177.0886, found 177.0887.

(*R*)-(3,4-dimethyl-2-(prop-1-en-2-yl)-2,5-dihydrofuran-2-yl)methanol (15d). This compound was obtained from **7d** (0.8 g) and purified by flash chromatography (hexanes/ ethyl ether 15:1). Yield: 0.29 g, 88%. Colorless oil. [α]_D²⁵ = -112.7 (c = 1.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 1.53 (s, 3H); 1.67 (s, 3H); 1.69 (s, 3H); 2.02 (s broad, 1H); 3.78 (m, 2H); 4.56 (m, 2H); 4.77 (s, 1H); 4.90 (s, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 9.2 (CH₃); 10.2 (CH₃); 19.0 (CH₃); 64.3 (CH₂); 78.8 (CH₂); 96.6 (C); 110.7 (CH₂); 127.8 (C); 130.0 (C); 145.3 (C). IR (film): 3440 (broad), 3085, 1640, 900, 850, 680 cm⁻¹. HRMS calcd for C₁₀H₁₆NaO₂ [M + Na]⁺ 191.1043, found 191.1049.

(*R*)-(2-allyl-3,6-dihydro-2*H*-pyran-2-yl)methanol (15e). This compound was obtained from **7e** (0.75 g) and purified

by flash chromatography (hexanes/ ethyl ether 15:1). Yield: 0.20 g, 68%. Colorless oil. [α]_D²⁵ = +42.2 (c = 1.0, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 1.61 (m, 1H); 2.14 (m, 1H); 2.28-2.49 (m, 3H); 3.52 (s, 2H); 4.12-4.25 (m, 2H); 5.08-5.31 (m, 2H); 5.89-5.70 (m, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 28.4 (CH₂); 37.8 (CH₂); 60.8 (CH₂); 66.0 (CH₂); 73.7 (C); 118.2 (CH₂); 122.5 (CH); 124.8 (CH); 133.3 (CH). IR (film): 3435 (broad), 1640, 1100, 740, 655 cm⁻¹. HRMS calcd for C₉H₁₄NaO₂ [M + Na]⁺ 177.0886, found 177.0884.

(*R*)-(4-methyl-2-(2-methylallyl)-3,6-dihydro-2*H*-pyran-2-yl)methanol (15f). This compound was obtained from **7f** (0.8 g) and purified by flash chromatography (hexanes/ ethyl ether 15:1). Yield: 0.25 g, 73%. Colorless oil. [α]_D²⁵ = +37.7 (c = 0.6, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 1.71 (d, *J* = 1.2 Hz, 3H); 1.82 (s, 3H); 1.88-2.07 (m, 3H); 2.29 (d, *J* = 13.6 Hz, 1H)-2.36 (d, *J* = 13.6 Hz, 1H); 3.55 (m, 2H); 4.14-4.23 (m, 2H); 4.76 (m, 1H); 4.89 (m, 1H); 5.41 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 23.3 (CH₃); 24.4 (CH₃); 33.7 (CH₂); 41.5 (CH₂); 61.1 (CH₂); 66.1 (CH₂); 74.5 (C); 115.0 (CH₂); 118.1 (CH); 130.1 (C); 142.2 (C). IR (film): 3450 (broad), 3070, 1640, 890, 770 cm⁻¹. HRMS calcd for C₁₁H₁₈NaO₂ [M + Na]⁺ 205.1199, found 205.1204.

(*R*)-(4,5-dimethyl-2-(2-methylallyl)-3,6-dihydro-2*H*-pyran-2-yl)methanol (15g). This compound was obtained from **13** (0.65 g) and purified by flash chromatography (hexanes/ ethyl ether 15:1). Yield: 0.18 g, 63%. Colorless oil. [α]_D²⁵ = +28.8 (c = 0.8, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 1.55 (s, 3H); 1.65 (m, 3H); 1.82 (m, 3H); 1.89-2.08 (m, 3H); 2.26 (d, *J* = 13.6 Hz, 1H); -2.35 (d, *J* = 13.6 Hz, 1H); 3.47-3.51 (m, 2H); 4.97-4.99 (m, 2H); 4.76 (m, 1H); 4.89 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 13.7 (CH₃); 18.6 (CH₃); 24.4 (CH₃); 34.6 (CH₂); 41.5 (CH₂); 64.8 (CH₂); 65.9 (CH₂); 74.9 (C); 114.9 (CH₂); 121.9 (C); 122.6 (C); 142.3 (C). IR (film): 3450 (broad), 3070, 1640, 890 cm⁻¹. HRMS calcd for C₁₂H₂₀NaO₂ [M + Na]⁺ 219.1356, found 219.1353.

(1*R*,2*S*,5*R*)-2-(2-((*R*,*Z*)-3-methoxy-5-methyl-3-(2-methylallyl)-3,4,7,8-tetrahydroazocin-1(2*H*)-yl)propan-2-yl)-5-methylcyclohexan-1-ol (28). To a suspension of LiAlH₄ (0.30 g, 7.9 mmol) in anhydrous THF (20 mL) cooled to -10 °C and under nitrogen atmosphere was added, in portions, dry AlCl₃ (0.35 g, 2.6 mmol). The mixture was stirred for 15 min at -10 °C and a solution of **24e** (0.75g, 2.1 mmol) in dry THF (15 mL) was slowly added. The reaction mixture was stirred at room temperature until disappearance of the starting product (TLC) and then it was quenched by addition of 10 % aqueous solution of NaOH (1.5 mL). The resulting mixture was filtered, the solid was washed with hot ethyl acetate, and the organic layer was dried over anhydrous MgSO₄. The solvent was eliminated under reduced pressure. The residue was purified by flash chromatography (hexanes/ ethyl acetate 2:1). Yield: 0.69 g, 92% White solid. Mp 94-96 °C (from pentane). [α]_D²⁵ = -35.1 (c = 1.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃, 333K): δ 0.82-1.06 (m, 2H); 0.90 (d, *J* = 6.5 Hz, 3H); 0.91 (s, 3H); 1.17 (s, 3H, CH₃); 1.38 (m, 1H); 1.52-1.81 (m, 3H); 1.77 (s, 3H); 1.81 (s, 3H); 1.93 (m, 1H); 2.02-2.19 (m, 2H); 2.2-2.48 (m, 5H); 3.20 (m, 1H); 3.23 (s, 3H); 3.62 (td, *J*₁ = 10.1 Hz, *J*₂ = 3.9 Hz, 1H); 4.88 (m, 1H); 4.95 (m, 1H); 5.52 (m, 1H); 7.50 (s broad, 1H). ¹³C NMR (75 MHz, CDCl₃, 333K): δ 20.2 (CH₃); 21.9 (2 CH₃); 24.2 (CH₃); 25.5 (CH₃); 26.6 (CH₂); 28.5 (CH₂); 31.0 (CH); 35.3 (CH₂); 37.9 (CH₂); 40.4 (CH₂); 44.7 (CH₂); 48.1 (CH); 48.7 (CH₃); 51.8 (CH₂); 55.3 (CH₂); 63.4 (C); 72.3 (CH); 80.6 (C); 113.9 (CH₂); 124.5 (CH); 137.0 (C); 141.8 (C). IR (nujol dispersion): 3170 (broad); 3075, 1640, 740 cm⁻¹. HRMS calcd for C₂₃H₄₂NO₂ [M + H]⁺ 364.3210, found 364.3218.

General method for elimination of the chiral auxiliary in 25a, 24b, 22c, 24c, 25d and 24e. To a suspension of LiAlH₄ (0.30 g, 7.9 mmol) in anhydrous THF (20 mL) cooled to -10 °C and under nitrogen atmosphere was added, in portions, dry AlCl₃ (0.35 g, 2.6 mmol). The mixture was

stirred for 15 min at -10°C and a solution of the corresponding benzoxazine (2.0 mmol) in dry THF (15 mL) was slowly added. The reaction mixture was stirred at room temperature until disappearance of the starting product by TLC (for reduction of **24b** it was necessary to heat to 60 °C), and then it was quenched by addition of 10 % aqueous solution of NaOH (1.5 mL). The resulting mixture was filtered, the solid was washed with hot ethyl acetate, and the organic layer was dried over anhydrous MgSO₄. The solvent was eliminated under reduced pressure, the residue was redissolved in anhydrous CH₂Cl₂ (30 mL), and PCC (1.8 g, 8.0 mmol) and 3 Å molecular sieves (4.0 g) was added to this solution. The mixture was stirred under nitrogen atmosphere until the oxidation was finished (TLC). The mixture was then treated with a 10 % aqueous solution of NaOH (50 mL) and extracted with CHCl₃ (5 x 25 mL). The organic phase was washed with brine, dried over anhydrous MgSO₄ and the solvent were removed under reduced pressure. The residue was redissolved in THF (30 mL) and MeOH (15 mL), an aqueous solution of KOH 2.5M (15 mL) was added and the mixture stirred at room temperature for 5-6 h. After elimination of the THF and MeOH under reduced pressure, the residue was acidified with a 1 M solution of HCl to pH 2 and extracted twice with Et₂O (2 x 20 mL). The aqueous solution was neutralized to pH 12 with a 10% aqueous solution of NaOH and extracted with CHCl₃ (4 x 20 mL). The organic layer was washed with brine, dried over MgSO₄, and the solvent eliminated under vacuum and the residue was purified by flash chromatography.

(R)-4-methyl-3-(prop-1-en-2-yl)-1,2,3,6-tetrahydropyridin-3-ol (29). This compound was obtained from **24b** (0.65 g) and purified by flash chromatography (CHCl₃/ MeOH 15:1). Yield: 0.19 g, 60%. Colorless oil. $[\alpha]_D^{25} = -10.5$ (c = 0.8, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 1.62 (d, J = 0.8 Hz, 3H); 1.70 (s, 3H, CH₃); 2.29 (d, J = 12.8 Hz, 1H); 2.96 (d, J = 12.8 Hz, 1H); 2.90-3.00 (m, 2H); 3.28-3.29 (m, 2H); 5.01 (m, 1H); 5.15 (m, 1H); 5.64 (m, 1H). ¹³C NMR (75 MHz, CDCl₃, 333K): δ 17.3 (CH₃); 18.9 (CH₃); 45.1 (CH₂); 54.1 (CH₂); 73.8 (C); 112.5 (CH₂); 124.9 (CH); 135.8 (C); 145.8 (C). IR (film): 3030 (broad), 3025, 1640, 740 cm⁻¹. HRMS calcd for C₉H₁₆NO [M + H]⁺ 154.1226, found 154.1230.

(R)-5-methyl-3-(2-methylallyl)-2,3,4,7-tetrahydro-1H-azepin-3-ol (30). This compound was obtained from **22c** (0.65 g) and purified by flash chromatography (CHCl₃/ MeOH 12:1). Yield: 0.21 g, 60%. Colorless oil. $[\alpha]_D^{25} = -75.8$ (c = 0.8, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃, 333K): δ 1.75 (s, 3H); 1.85 (s, 3H); 2.2 (s, 2H); 2.23 (d, J = 15.1 Hz, 1H); 2.36 (d, J = 15.1 Hz, 1H); 2.67 (s broad, 2H); 2.74 (d, J = 12.8 Hz, 1H); 2.98 (d, J₁ = 12.8 Hz, 1H); 3.21 (m, 1H); 3.32 (dd, J₁ = 15.4 Hz, J₂ = 7.0 Hz, 1H); 4.72 (d, 1H, J = 0.8 Hz); 4.87 (s, 1H); 5.65 (m, 1H). ¹³C NMR (75 MHz, CDCl₃, 333K): δ 24.5 (CH₃); 27.5 (CH₃); 45.7 (CH₂); 47.9 (CH₂); 48.5 (CH₂); 61.7 (CH₂); 69.7 (C); 114.7 (CH₂); 124.8 (CH); 136.7 (C); 142.6 (C). IR (film): 3330 (broad), 3070, 1645, 890 cm⁻¹. HRMS calcd for C₁₁H₂₀NO [M + H]⁺ 182.1539, found 182.1543.

(R)-3-methoxy-5-methyl-3-(2-methylallyl)-2,3,4,7-tetrahydro-1H-azepine (31). This compound was obtained from **24c** (0.85 g) and purified by flash chromatography (CHCl₃/ MeOH 15:1). Yield: 0.28 g, 59%. Colorless oil. $[\alpha]_D^{25} = +19.8$ (c = 1.0, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 1.73 (s, 3H); 1.75 (s, 3H); 2.8 (1H); 2.14 (d, J = 14.4 Hz, 1H); 2.21 (d, J = 14.4 Hz, 1H); 2.27 (d, J = 15.2 Hz, 1H); 2.40 (d, J = 15.2 Hz, 1H); 2.78 (d, J = 14.5 Hz, 1H); 3.04 (d, J = 15.5 Hz, 1H); 3.17 (m, 1H); 3.18 (s, 3H); 3.32 (dd, J₁ = 16.1 Hz, J₂ = 5.4 Hz, 1H); 4.70 (s, 1H); 4.81 (s, 1H); 5.49 (m, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 24.0 (CH₃); 27.0 (CH₃); 41.0 (CH₂); 42.3 (CH₂); 48.3 (CH₂); 49.2 (CH₃); 58.3 (CH₂); 77.0 (C); 114.5 (CH₂); 126.3 (CH); 134.8 (C); 142.0 (C). IR (film): 3380 (broad), 3075, 1645, 1460, 890 cm⁻¹. HRMS calcd for C₁₂H₂₂NO [M + H]⁺ 196.1696, found 196.1692.

(R, Z)-3-methoxy-5-methyl-3-(2-methylallyl)-1,2,3,4,7,8-hexahydroazocine (32). This compound was obtained from **24e** (0.75 g) and purified by flash chromatography (CHCl₃/ MeOH 20:1). Yield: 0.22 g, 52%. Colorless oil. $[\alpha]_D^{25} = -69.9$ (c = 1.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃, 300K): δ (s, 6H); 1.93-2.07 (m, 2H); 2.15 (d, J = 14.8 Hz, 1H); 2.17 (m, 1H); 2.21 (d, J = 13.4 Hz, 1H); 2.27 (d, J = 13.4 Hz, 1H); 2.28 (d, J = 14.8 Hz, 1H); 2.59, J = 14.4 Hz, 1H); 2.61 (m, H); 3.22 (s, 3H); 4.76 (d, J = 0.8 Hz, 1H); 4.83 (d, J = 0.8 Hz, 1H); 5.41 (m, 1H). ¹³C NMR (75 MHz, CDCl₃, 300K): δ 24.0 (CH₃); 26.3 (CH₃); 29.6 (CH₂); 38.3 (CH₂); 41.6 (CH₂); 48.9 (CH₃); 49.2 (CH₂); 53.3 (CH₂); 82.1 (C); 114.2 (CH₂); 123.8 (CH); 137.7 (C); 142.3 (C). IR (film): 3370 (ancho), 3075, 1640, 690 cm⁻¹. HRMS calcd for C₁₃H₂₄NO [M + H]⁺ 210.1852, found 210.1849.

(S)-3-methoxy-3-vinyl-1,2,3,6-tetrahydropyridine (33). This compound was obtained from **25a** (0.75 g) and purified by flash chromatography (CHCl₃/ MeOH 15:1). Yield: 0.20 g, 56%. Colorless oil. $[\alpha]_D^{25} = +52.1$ (c = 0.5, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 2.30 (broad, 1H); 2.69 (d, J = 13.2 Hz, 1H); 3.01 (d, J = 13.2 Hz, 1H); 3.21-3.38 (m, 2H); 3.24 (s, 3H); 5.21 (d, J = 17.6 Hz, 1H), 5.27 (d, J = 10.8 Hz, 1H); 5.80 (dd, J₁ = 17.6 Hz, J₂ = 10.8 Hz, 1H); 5.99 (m, 1H), 6.06 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 44.9 (CH₂); 50.7 (CH₃); 52.7 (CH₂); 72.6 (C); 116.9 (CH₂); 126.3 (CH); 132.4 (CH); 140.4 (CH). IR (film): 3320 (broad), 3085, 1635, 1460, 720, 685 cm⁻¹. HRMS calcd for C₈H₁₄NO [M + H]⁺ 140.1070, found 140.1071.

(S)-3-methoxy-3-vinyl-2,3,6,7-tetrahydro-1H-azepine (34). This compound was obtained from **25d** (0.65 g) and purified by flash chromatography (CHCl₃/ MeOH 15:1). Yield: 0.22 g, 68%. Colorless oil. $[\alpha]_D^{25} = -4.2$ (c = 1.2, CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 2.28-2.35 (m, 2H); 2.89-3.20 (m, 4H); 3.24 (s, 3H); 3.50 (broad, 1H); 5.27-5.36 (m, 2H); 5.70 (m, 2H); 6.05 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 30.7 (CH₂); 47.8 (CH₂); 50.9 (CH₃); 55.9 (CH₂); 77.00 (C); 117.6 (CH₂); 131.7 (CH); 133.1 (CH); 140.2 (CH). IR (film): 3410 (broad); 3085, 1640, 146, 755 cm⁻¹. HRMS calcd for C₉H₁₆NO [M + H]⁺ 154.1226, found 154.1228.

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