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Stereoselective Intramolecular Oxazine Formation by a π-Allylpalladium Complex Catalyzed by Pd^0

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An efficient procedure for synthesizing oxazines was developed by the palladium(0)-catalyzed intramolecular cyclization of a benzamide through a π-allylpalladium(II) complex. Unlike other palladium-catalyzed reactions, the temperature was found to be a key factor in determining the stereochemistry of the oxazine.

Introduction

Allylpalladium chemistry has become one of the most successful areas of organometallic catalysis due to its remarkable capacity for continuous renewal.[1] Catalytic transformations involving nucleophilic attack on (η^3-allyl)-palladium intermediates have been widely used in a number of important chemical processes including allylic substitution and the transformation of alkenes.[2]

The palladium(0)-catalyzed intramolecular cyclization of a benzamide through a π-allylpalladium(II) complex is useful for the synthesis of highly functionalized compounds, particularly when chirality transfer is involved.[3] A previous paper described a new procedure for the highly stereoselective formation of an oxazoline ring from an acyclic allylic amide possessing a benzoyl substituent as an *N*-protecting group in the presence of tetrakis(triphenylphosphane)palladium(0) and base (K_2CO_3). The synthetic utility of these oxazolines as chiral building blocks has been demonstrated by their successful application to the synthesis of β-amino-α-hydroxy and γ-amino-β-hydroxy acids[4] and biologically active natural products such as preussin,[5] sphingofungin F,[6] spectaline,[7] myriocin,[8] L-733060,[9] 1-deoxygalactonojirimycin,[10] and 1-deoxygulonojirimycin.[11]

As part of an ongoing program directed at expanding the scope of the palladium(0)-catalyzed intramolecular cyclization of benzamides through a π-allylpalladium(II) complex, this study examined the formation of oxazines from γ-allylbenzamides, which contain an additional carbon atom compared to the substrates used in the formation of oxazolines. This paper discusses the results of these reactions.

Results and Discussion

As a model study, we monitored the reactivity of compound **1a** and attempted to identify the optimum conditions for this unusual cyclization reaction. The necessary cyclization precursor **1a** was simply prepared from our oxazolines.[12]

The conditions for the cyclization of the oxazine precursor **1a** were investigated by examining the effects of the bases, ligands, and solvents as summarized in Table 1.

Unfortunately, most of the conditions did not work at all when the leaving group was acetate. However, in the case of chloride, the reaction proceeded sluggishly under the same conditions [$Pd(PPh_3)_4$, K_2CO_3, and CH_3CN] that were used in the formation of the oxazoline. The use of a much stronger base such as NaH improved the yield. Therefore, under the conditions of $Pd(PPh_3)_4$, NaH, and $n$$Bu_4NI$ in THF at room temp., the intramolecular cyclization afforded the oxazine **2a** as a 5:1 *syn*/*anti* mixture (as determined by ^1H NMR) in a moderate yield (59%).

These reaction conditions were then extended to other substrates used to investigate the influence of the R group on the reactivity. The substrates were synthesized according to the procedure shown in Scheme 1.

The ozonolysis of olefins **3a**–**d** and their subsequent Horner–Wadsworth–Emmons reaction afforded the α,β-unsaturated esters **4a**–**d** with good (*E*)/(*Z*) selectivity (>15:1 as determined by ^1H NMR). The reduction of compounds **4a**–**d** by DIBALH at –78 °C produced the corresponding allylic alcohols **5a**–**d** in high yield. The conversion of these alcohols to chlorides and the subsequent acid-catalyzed hydrolysis of the oxazolines, followed by the addition of sodium hydrogencarbonate to increase the pH of the reaction mixture to 9.0, furnished the *syn*-amino alcohols **7a**–**d**.[13] The protection of the resulting alcohols by TBDMSCl afforded the cyclization precursors **1a**–**d** in good yield.

The application of the same method to compound **1** with benzyl, isopropyl, isobutyl and cyclohexylmethyl as the sub-

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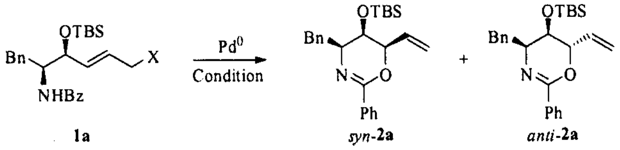
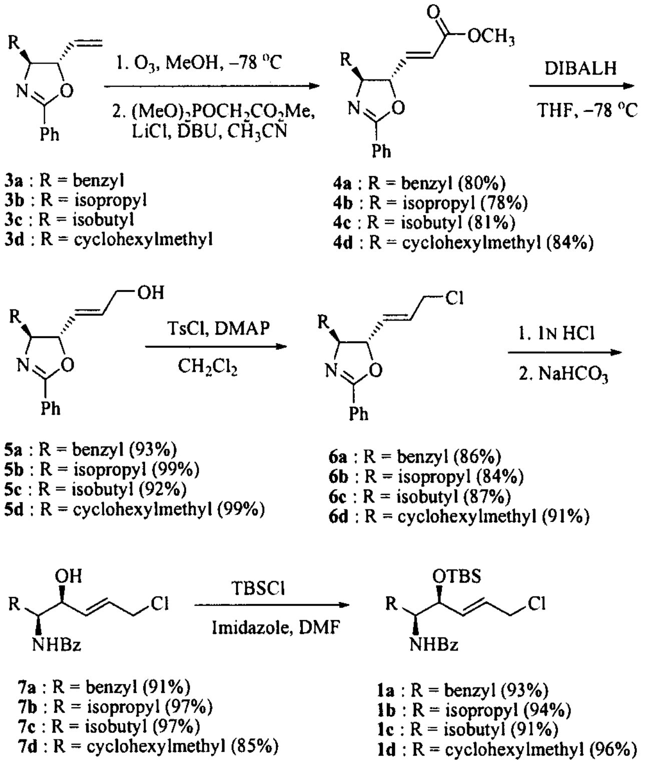
Table 1. Oxazine formation catalyzed by Pd^0.



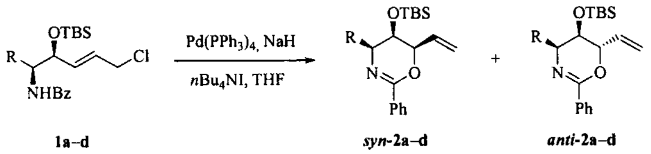
X	Pd^{0}[a]	Conditions[b]	Yield [%][c]	*syn*/*anti*[d]
OAc	Pd_2dba_3, dppe	K_2CO_3, CH_3CN, reflux, 24 h	no reaction	–
OAc	Pd_2dba_3, dppe	NaH, THF, room temp., 24 h	no reaction	–
OAc	$Pd(PPh_3)_4$	K_2CO_3, CH_3CN, reflux, 24 h	no reaction	–
OAc	$Pd(PPh_3)_4$	NaH, THF, room temp., 24 h	low	–
Cl	Pd_2dba_3, dppe	K_2CO_3, CH_3CN, reflux, 12 h	low	–
Cl	Pd_2dba_3, dppe	NaH, THF, room temp., 12 h	low	–
Cl	$Pd(PPh_3)_4$	K_2CO_3, CH_3CN, reflux, 12 h	15	3.1:1
Cl	$Pd(PPh_3)_4$	NaH, THF, room temp., 12 h	40	4.5:1
Cl	$Pd(PPh_3)_4$	NaH, *n*Bu_4NI, THF, room temp., 12 h	59	5:1

[a] Pd^0 was used as follows: $Pd(PPh_3)_4$ (0.2 equiv.) or Pd_2dba_3 (0.1 equiv.) in the presence or absence of dppe (0.4 equiv.). [b] Base was used as follows: NaH (2 equiv.) or K_2CO_3 (2 equiv.). [c] Yields refer to pure products or product mixtures (*syn*/*anti*). [d] Ratio was determined by ^1H NMR spectroscopy.



Scheme 1.

Table 2. Oxazine formation from various substrates.[a]



Allyl chloride	Temp.	Time [h]	Yield [%][b]	*syn*/*anti*[c]
1a	0 °C	5	80	8.3:1
1a	room temp.	12	59	5:1
1a	40 °C	12	68	1:15.2
1b	0 °C	5	73	13.4:1
1b	room temp.	12	64	1:9
1b	40 °C	12	77	1:16
1c	0 °C	5	88	9:1
1c	room temp.	12	76	1:1.4
1c	40 °C	12	72	1:7.5
1d	0 °C	5	89	14:1
1d	room temp.	12	66	4.4:1
1d	40 °C	12	73	1:8.5

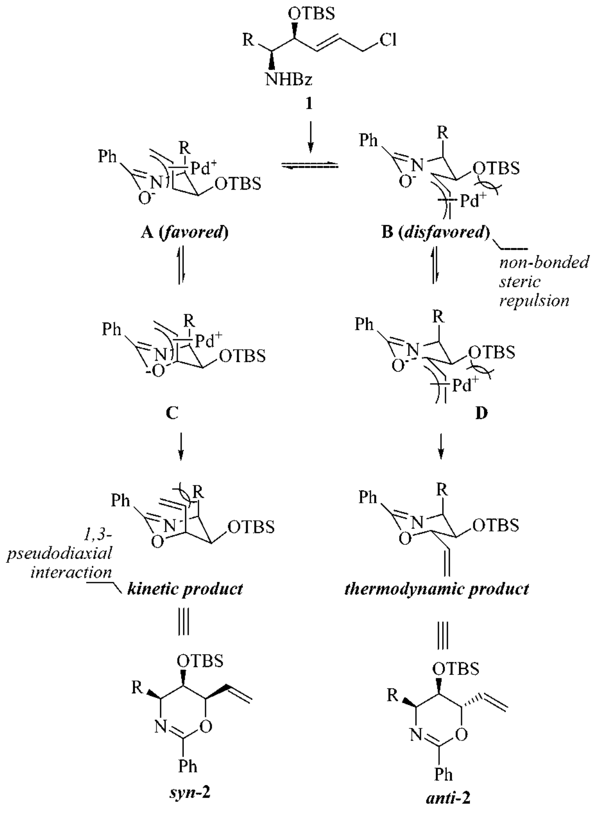
[a] Reaction conditions: $Pd(PPh_3)_4$ (0.2 equiv.), NaH (2 equiv.), *n*Bu_4NI (1 equiv.), and THF. [b] Yields refer to pure products or product mixtures. [c] Ratio was determined by ^1H NMR spectroscopy.

stituent group afforded the corresponding oxazines **2a**–**d** in moderate to good yields and diastereoselectivities as summarized in Table 2.

The reaction at room temp. showed a different selectivity depending on the R groups. However, it should be noted that when the reaction temperature was increased to 40 °C, a drastic change was observed in the diastereoselectivity, particularly in the case of benzyl and cyclohexylmethyl as the substituents, where the *anti* adducts were obtained as the major isomers. In contrast, when the same reaction was performed at 0 °C, in which a possible inversion of the selectivity observed under cold reaction conditions was anticipated, the *syn* products were produced as major isomers. It is interesting that the palladium-catalyzed reaction is so dependent on the temperature. To the best of our knowledge, there is no example of a palladium-catalyzed reaction that shows a drastic stereochemical change that depends on the reaction temperature ranging in the range 0–40 °C.

A possible explanation for the stereoselective formation of *syn*-**2** or *anti*-**2** is as follows (Scheme 2). The chair-like transition states **A** and **B** which have the bulky *tert*-butyldimethylsilyloxy (TBDMSO) group in an equatorial orientation to minimize the conformational energy, are proposed to explain the stereochemical outcome of the cyclization.

The initial π-allylpalladium complexes **A** and **B** were equilibrated by π-σ-π isomerization.[14] Although the axially disposed π-allylpalladium complex in transition state **A** might suffer from a non-bonding gauche repulsion with the TBDMSO group, transition state **B** appears to be further destabilized by non-bonded steric repulsion between the equatorial π-allylpalladium complex and the TBDMSO group. It is reasonable to assume that the formation of transition state **C** followed by the intramolecular cyclization to *syn*-**2** is kinetically preferred due to the non-bonded steric repulsion in transition state **B**. This appears to be the reason why the kinetic product *syn*-**2** was obtained at 0 °C. On the other hand, the observed stereochemical outcome at 40 °C can be regarded to be a consequence of the selective formation of transition state **D**. Although it is more difficult to overcome the higher energy barrier for the formation of transition state **D** than that of transition state **C**, once this barrier is overcome, the thermodynamic product *anti*-**2** is preferred because it is more stable than *syn*-**2**, which is thermodynamically not favored due to the presumed 1,3-pseudodiaxial interaction between the vinyl and R groups.



Scheme 2.

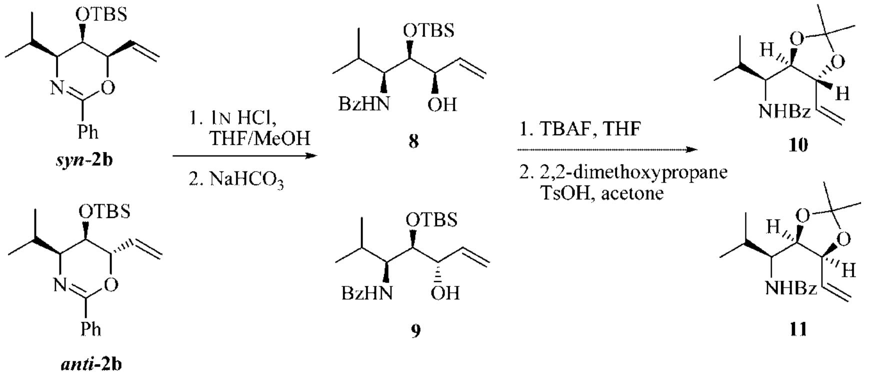
At room temp., the presumed 1,3-diaxial interaction in transition state **C** could compete with the non-bonded steric repulsion in transition state **B**. This rationale is partly supported by the relatively high *anti* stereoselectivities (thermodynamic product formation) at room temp. in the more bulky precursors (where R = isopropyl or isobutyl).

In order to confirm the role of the TBDMSO group in stereoselectivity, (*E*,*R*)-*N*-(6-chloro-1-phenylhex-4-en-2-yl)-benzamide was prepared from L-phenylalanine. The exposure of allyl chloride lacking the bulky TBDMSO group to the same conditions for oxazine formation resulted in an approximately 1:1 mixture of the *syn*- and *anti*-oxazines in 57% yield. This result verified that the bulky TBDMSO group plays an important role in determining the stereoselectivity during oxazine formation.

Although it is difficult to fully rationalize these results at this stage, this phenomenon is beneficial from a synthetic viewpoint because one can take advantage of the unique amino alcohol moiety present in the oxazines for the synthesis of natural products.

To verify the stereochemical outcome of the newly generated stereocenter, C-6, the oxazines were transformed into their acetonides because the coupling constants of 4-H, 5-H, and 6-H obtained for the oxazines did not provide concrete information as to their stereochemistry. This was accomplished by hydrolyzing the oxazine ring to the benzoylamino alcohol by a simple treatment with 3 N HCl, and the TBDMSO group was then removed with TBAF to give the diol. The resulting diol was protected as the acetonide by a reaction with 2,2-dimethoxypropane and TsOH in acetone (Scheme 3).

Initially, the coupling constants of 3-H and 4-H in the acetonides were determined, but unfortunately, they had similar values of 8.5 Hz and 7.5 Hz. Therefore, the NOE spectrum was studied under the assumption that there must be an NOE difference between the two isomers because in the case of the *cis*-acetonide, 3-H and 4-H are on the same



Scheme 3.

side. It was expected that both protons would show a similar NOE with the neighboring methyl group [CH_3(b)] but not with the methyl group [CH_3(a)] on the opposite side. However, in the *trans*-acetonide, each proton (3-H and 4-H) had a single NOE with the methyl group sharing the same space (Figure 1).

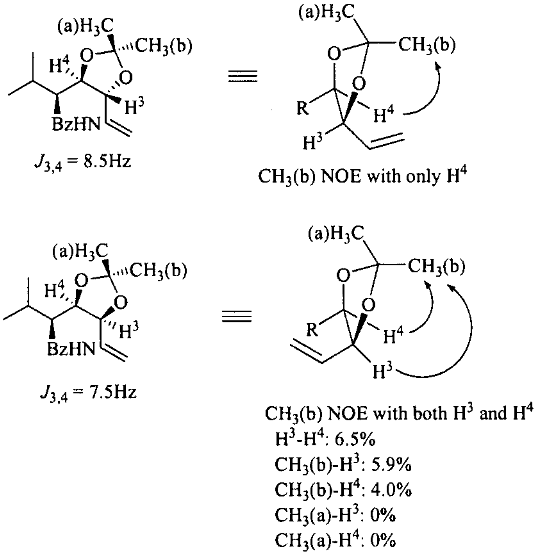


Figure 1. Observed NOEs in acetonides **10** and **11**.

A similar increase in the NOE value of CH_3(b)–3-H and CH_3(b)–4-H of the *cis*-acetonide was observed, but there were no NOEs involving CH_3(a). Unfortunately, the NOE experiment for the *trans*-acetonide was unsuccessful because the chemical shifts of 3-H and 4-H are almost the same. However, the NOE for the *cis*-acetonide was sufficient to verify the stereochemistry of the oxazines.

Conclusions

This study developed an efficient procedure for synthesizing oxazines by a palladium(0)-catalyzed intramolecular cyclization of benzamides through a π-allylpalladium(II) complex. It should be noted that unlike other palladium-catalyzed reactions, temperature is the critical factor in determining the stereochemistry of the oxazine. A means of generating an alcohol moiety stereoselectively in the γ-position of the amine is important from a synthetic point of view. Studies examining the reactivity and stereoselectivity during the formation of the oxazine when various alkyl groups are substituted for the TBDMSO group are currently underway.

Experimental Section

General: Optical rotations were measured with a JASCO DIP 1020 digital polarimeter. ^{1}H and ^{13}C NMR spectra were recorded with a Varian INOVA FT-NMR spectrometer at 500 and 125 MHz, respectively, in $CDCl_3$. Chemical shifts are reported as δ values in ppm relative to $CHCl_3$ ($\delta = 7.26$ ppm) in $CDCl_3$. IR spectra were measured with a Bruker FT-IR spectrometer. High-resolution mass spectra were recorded with a JMS-700 Mstation. Flash chromatography was executed with Merck Kiesegel 60 (230–400 mesh) with mixtures of ethyl acetate and hexane as eluents. Ethyl acetate and hexane were dried and purified by distillation prior to use. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium and benzophenone (indicator). Dichloromethane (CH_2Cl_2) was shaken with concentrated sulfuric acid, dried with potassium carbonate, and distilled. Commercially available compounds were used without further purification.

Methyl (*E*)-3-[(4*S*,5*S*)-4-Benzyl-4,5-dihydro-2-phenyloxazol-5-yl]-acrylate (4a): Oxazoline **3a** (6.78 mmol, 1 equiv.) was dissolved in dry methanol (50 mL) and cooled to –78 °C. Ozonized oxygen was bubbled into the solution until the reaction was complete. The reaction mixture was quenched with $(CH_3)_2S$ (1.0 mL) and warmed to room temp. The solvents were evaporated under reduced pressure. The crude aldehyde was immediately employed in the next step without further purification. To a stirred solution of LiCl (0.34 g, 8.14 mmol, 1.2 equiv.) in CH_3CN (80 mL), were added trimethylphosphonoacetate (1.18 mL, 8.14 mmol, 1.2 equiv.) and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.01 mL, 6.78 mmol, 1 equiv.), and stirring was continued for 1 h. The crude aldehyde in CH_3CN (10 mL) was added, and the reaction mixture was stirred for 2 h. The reaction mixture was poured into H_2O (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo. Purification by silica gel chromatography (ethyl acetate/hexane = 1:6) gave (*E*)-α,β-unsaturated ester **4a** in 80% yield (2 steps); colorless oil. $[\alpha]_D^{20} = +106.7$ ($c = 1.0$, $CHCl_3$). IR (neat): $\tilde{\nu} = 3027, 2948, 1725, 1651, 1322\ 1274\ cm^{-1}$. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.76$ (dd, $J = 13.5, 9$ Hz, 1 H), 3.30 (dd, $J = 13.5, 5$ Hz, 1 H), 3.68 (s, 3 H), 4.32 (ddd, $J = 9, 6.5, 5$ Hz, 1 H), 4.89 (ddd, $J = 6.5, 5, 1.5$ Hz, 1 H), 5.80 (dd, $J = 15.5, 1.5$ Hz, 1 H), 6.65 (dd, $J = 15.5, 5$ Hz, 1 H), 7.24–7.34 (m, 5 H), 7.40–7.44 (m, 2 H), 7.48–7.50 (m, 1 H), 7.96–7.98 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 42.2$, 52.4, 74.6, 82.6, 121.3, 127.6, 127.9, 129.05, 129.17, 129.46, 130.1, 132.4, 137.6, 145.8, 163.6, 166.9 ppm. According to the procedure described above for the ester **4a**, olefins **3b**–**d** were converted into esters **4b**–**d**.

Methyl (*E*)-3-[(4*S*,5*S*)-4,5-Dihydro-4-isopropyl-2-phenyloxazol-5-yl]acrylate (4b): 78% yield (2 steps); colorless oil. $[\alpha]_D^{20} = +115.2$ ($c = 1.0$, $CHCl_3$). IR (neat): $\tilde{\nu} = 2956, 1727, 1655, 1450, 1274, 1193\ cm^{-1}$. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.97$ (d, $J = 6.5$ Hz, 3 H), 1.05 (d, $J = 6.5$ Hz, 3 H), 1.95 (m, $J = 6.5, 6.5, 6.5$ Hz, 1 H), 3.74 (s, 3 H), 3.88 (dd, $J = 6.5, 6.5$ Hz, 1 H), 4.92 (ddd, $J = 6.5, 5, 1.5$ Hz, 1 H), 6.08 (dd, $J = 15.5, 1.5$ Hz, 1 H), 6.94 (dd, $J = 15.5, 5$ Hz, 1 H), 7.40–7.44 (m, 2 H), 7.48–7.51 (m, 1 H), 7.97–7.99 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 18.7$, 19.4, 52.5, 79.3, 80.7, 121.3, 128.1, 129.0, 129.1, 132.2, 146.6, 162.8, 167.1 ppm.

Methyl (*E*)-3-[(4*S*,5*S*)-4,5-Dihydro-4-isobutyl-2-phenyloxazol-5-yl]-acrylate (4c): 81% yield (2 steps); colorless oil. $[\alpha]_D^{20} = +67.2$ ($c = 1.0$, $CHCl_3$). IR (neat): $\tilde{\nu} = 2955, 1727, 1654, 1450, 1367, 1321, 1171\ cm^{-1}$. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.98$ (d, $J = 6.5$ Hz, 3 H), 1.00 (d, $J = 6.5$ Hz, 3 H), 1.46 (ddd, $J = 6.5, 6.5, 6.5$ Hz, 1 H), 1.68 (ddd, $J = 6.5, 6.5, 6.5$ Hz, 1 H), 1.90 (m, 1 H), 3.76 (s, 3 H), 4.09 (ddd, $J = 6.5, 6.5, 6.5$ Hz, 1 H), 4.78 (ddd, $J = 6.5, 5.5, 1.5$ Hz, 1 H), 6.10 (dd, $J = 15.5, 1.5$ Hz, 1 H), 6.98 (dd, $J = 15.5, 5.5$ Hz, 1 H), 7.40–7.43 (m, 2 H), 7.47–7.49 (m, 1 H), 7.95–7.97 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 26.83$, 26.85, 27.19, 34.10, 34.20, 35.17, 44.7, 52.5, 71.1, 84.2, 121.6, 128.10, 128.98, 129.09, 132.20, 145.7, 163.0, 167.0 ppm.

Methyl (*E*)-3-[(4*S*,5*S*)-4-(Cyclohexylmethyl)-4,5-dihydro-2-phenyloxazol-5-yl]acrylate (4d): 84% yield (2 steps); colorless oil. $[\alpha]_D^{20}$

= +44.7 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2923, 1727, 1654, 1448, 1372, 1271 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.96–0.99 (m, 2 H), 1.16–1.28 (m, 3 H), 1.42–1.45 (m, 1 H), 1.50–1.64 (m, 1 H), 1.66–1.73 (m, 4 H), 1.79–1.80 (m, 2 H), 3.76 (s, 3 H), 4.12 (ddd, *J* = 7, 7, 7 Hz, 1 H), 4.78 (ddd, *J* = 7, 5.5, 1.5 Hz, 1 H), 6.09 (dd, *J* = 15.5, 1.5 Hz, 1 H), 6.97 (dd, *J* = 15.5, 5.5 Hz, 1 H), 7.40–7.43 (m, 2 H), 7.47–7.49 (m, 1 H), 7.95–7.97 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.40, 23.52, 25.8, 46.0, 52.5, 71.7, 84.1, 121.7, 128.10, 128.97, 129.08, 132.19, 145.7, 162.9, 167.0 ppm.

(*E*)-3-[(4*S*,5*S*)-4-Benzyl-4,5-dihydro-2-phenyloxazol-5-yl]prop-2-en-1-ol (5a): *i*Bu_2AlH (1.0 M solution in hexane (13.13 mL, 13.13 mmol, 3 equiv.) was added to a solution of the α,β-unsaturated ester **4a** (4.38 mmol, 1 equiv.) in dry THF (25 mL) at –78 °C. The reaction mixture was stirred at –78 °C for 2 h and diluted with Et_2O (25 mL) and saturated aqueous NH_4Cl (5 mL). After being stirred at room temp. for 2 h, the resulting suspension was filtered through a Celite pad. The filtrate was concentrated in vacuo to give the crude product, which upon purification by column chromatography on silica gel (ethyl acetate/hexane = 1:2) gave the allylic alcohol **5a** in 93% yield; colorless oil. $[\alpha]_D^{20}$ = +15.4 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 3271, 1644, 1495, 1450, 1331 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.76 (dd, *J* = 13.5, 8.5 Hz, 1 H), 3.24 (dd, *J* = 13.5, 5.5 Hz, 1 H), 4.01 (m, 2 H), 4.23 (ddd, *J* = 8.5, 7, 5.5 Hz, 1 H), 4.78 (dd, *J* = 7, 6 Hz, 1 H), 5.57–5.66 (m, 2 H), 7.20–7.31 (m, 5 H), 7.39–7.50 (m, 3 H), 7.94–7.96 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 42.2, 63.0, 74.3, 84.8, 127.31, 128.23, 129.02, 129.09, 129.20, 129.22, 130.26, 132.23, 132.91, 138.1, 164.0 ppm. According to the procedure described above for the alcohol **5a**, esters **4b–d** were converted into alcohols **5b–d**.

(*E*)-3-[(4*S*,5*S*)-4,5-Dihydro-4-isopropyl-2-phenyloxazol-5-yl]prop-2-en-1-ol (5b): 99% yield; colorless oil. $[\alpha]_D^{20}$ = –23.4 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 3273, 1646, 1450, 1343 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 6.5 Hz, 3 H), 1.02 (d, *J* = 6.5 Hz, 3 H), 1.90 (m, 1 H), 3.80 (dd, *J* = 6.5, 6.5 Hz, 1 H), 4.20 (dd, *J* = 5, 1.5 Hz, 2 H), 4.82 (ddd, *J* = 6.5, 6.5, 0.5 Hz, 1 H), 5.82 (dddd, *J* = 15, 6.5, 1.5, 1.5 Hz, 1 H), 5.96 (dddd, *J* = 15, 5, 5, 0.5 Hz, 1 H), 7.39–7.42 (m, 2 H), 7.46–7.49 (m, 1 H), 7.95–7.98 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.83, 19.39, 33.3, 63.3, 79.1, 82.6, 128.46, 128.98, 129.00, 130.61, 131.98, 132.43, 163.1 ppm.

(*E*)-3-[(4S,5S)-4,5-Dihydro-4-isobutyl-2-phenyloxazol-5-yl]prop-2-en-1-ol (5c): 92% yield; colorless oil. $[\alpha]_D^{20}$ = –40.9 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 3272, 2955, 1645, 1450, 1330 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.98 (m, 6 H), 1.41 (ddd, *J* = 7, 7, 7 Hz, 1 H), 1.64 (ddd, *J* = 7, 7, 7 Hz, 1 H), 1.89 (m, 1 H), 4.00 (ddd, *J* = 7, 7, 7 Hz, 1 H), 4.20 (dd, *J* = 5, 1.5 Hz, 2 H), 4.67 (ddd, *J* = 7, 7, 0.5 Hz, 1 H), 5.85 (dddd, *J* = 15, 7, 1.5, 1.5 Hz, 1 H), 5.96 (dddd, *J* = 15, 5, 5, 0.5 Hz, 1 H), 7.40 (m, 2 H), 7.46 (m, 1 H), 7.95 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.47, 23.58, 25.68, 45.89, 63.13, 71.45, 86.17, 128.47, 128.96, 129.02, 129.48, 132.02, 133.27, 163.29 ppm.

(*E*)-3-[(4*S*,5*S*)-4-(Cyclohexylmethyl)-4,5-dihydro-2-phenyloxazol-5-yl]prop-2-en-1-ol (5d): 99% yield; colorless oil. $[\alpha]_D^{20}$ = –43.9 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 3274, 2921, 1644, 1448, 1333 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.94–0.97 (m, 2 H), 1.15–1.29 (m, 3 H), 1.38–1.42 (m, 1 H), 1.51–1.60 (m, 1 H), 1.61–1.72 (m, 4 H), 1.75–1.79 (m, 2 H), 4.02 (ddd, *J* = 7, 7, 7 Hz, 1 H), 4.18 (dd, *J* = 5, 1.5 Hz, 2 H), 4.66 (ddd, *J* = 7, 7, 0.5 Hz, 1 H), 5.81 (dddd, *J* = 15, 7, 1.5, 1.5 Hz, 1 H), 5.94 (dddd, *J* = 15, 5, 5, 0.5 Hz, 1 H), 7.38–7.41 (m, 2 H), 7.44–7.48 (m, 1 H), 7.93–7.95 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.86, 26.89, 27.23, 44.5, 63.0, 70.7, 86.2, 128.39, 128.97, 129.02, 129.25, 132.05, 133.35, 163.4 ppm.

(4*S*,5*S*)-4-Benzyl-5-[(*E*)-3-chloroprop-1-enyl]-4,5-dihydro-2-phenyloxazole (6a): *p*-Toluenesulfonyl chloride (6.38 g, 33.45 mmol, 10 equiv.) and 4-(dimethylamino)pyridine (2.04 g, 16.73 mmol, 5 equiv.) were added to a stirred solution of allylic alcohol **5a** (3.35 mmol, 1 equiv.) in dry CH_2Cl_2 (35 mL) at room temp., and stirring was continued for 24 h. The reaction mixture was quenched with H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo. Purification by silica gel chromatography (ethyl acetate/hexane = 1:6) gave allyl chloride **6a** in 86% yield; colorless oil. $[\alpha]_D^{20}$ = +25.6 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 1649, 1494, 1450, 1328, 1061 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.76 (dd, *J* = 13.5, 8.5 Hz, 1 H), 3.29 (dd, *J* = 13.5, 5.5 Hz, 1 H), 3.93 (m, 2 H), 4.26 (ddd, *J* = 8.5, 7, 5.5 Hz, 1 H), 4.77 (dd, *J* = 7, 6 Hz, 1 H), 5.62 (m, 2 H), 7.22–7.33 (m, 5 H), 7.40–7.51 (m, 3 H), 7.95–7.98 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 42.15, 44.48, 74.51, 83.95, 127.40, 128.22, 128.54, 129.02, 129.10, 129.30, 130.17, 132.24, 133.02, 137.89, 163.70 ppm. According to the procedure described above for the allylic chloride **6a**, alcohols **5b–d** were converted into allylic chlorides **6b–d**.

(4*S*,5*S*)-5-[(*E*)-3-Chloroprop-1-enyl]-4,5-dihydro-4-isopropyl-2-phenyloxazole (6b): 84% yield; colorless oil. $[\alpha]_D^{20}$ = +0.7 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2958, 1652, 1449, 1327, 1249, 1062 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 6.5 Hz, 3 H), 1.01 (d, *J* = 6.5 Hz, 3 H), 1.92 (m, 1 H), 3.81 (dd, *J* = 6.5, 6.5 Hz, 1 H), 4.08 (m, 2 H), 4.81 (dd, *J* = 6.5, 6.5 Hz, 1 H), 5.85–5.97 (m, 2 H), 7.40–7.43 (m, 2 H), 7.47–7.50 (m, 1 H), 7.96–7.98 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.81, 19.41, 33.3, 44.6, 79.1, 82.0, 128.34, 128.55, 129.00, 129.02, 132.04, 134.10, 162.94 ppm.

(4*S*,5*S*)-5-[(*E*)-3-Chloroprop-1-enyl]-4,5-dihydro-4-isobutyl-2-phenyloxazole (6c): 87% yield; colorless oil. $[\alpha]_D^{20}$ = –20.9 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2955, 1650, 1450, 1325, 1060 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.96–1.00 (m, 6 H), 1.42 (m, 1 H), 1.66 (m, 1 H), 1.89 (m, 1 H), 4.01 (dd, *J* = 14.5, 7.0 Hz, 1 H), 4.08 (m, 2 H), 4.66 (dd, *J* = 7.0, 7.0 Hz, 1 H), 5.93 (m, 2 H), 7.38–7.40 (m, 2 H), 7.46–7.49 (m, 1 H), 7.94–7.96 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.9, 23.2, 25.3, 44.1, 45.4, 71.2, 85.0, 128.0, 128.5, 128.6, 128.7, 131.6, 132.8, 162.6 ppm.

(4*S*,5*S*)-5-[(*E*)-3-Chloroprop-1-enyl]-4-(cyclohexylmethyl)-4,5-dihydro-2-phenyloxazole (6d): 91% yield; colorless oil. $[\alpha]_D^{20}$ = –43.3 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2921, 1650, 1448, 1329, 1061 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.95–0.99 (m, 2 H), 1.16–1.31 (m, 3 H), 1.40–1.44 (m, 1 H), 1.54–1.58 (m, 1 H), 1.65–1.73 (m, 4 H), 1.77–1.82 (m, 2 H), 4.03–4.10 (m, 3 H), 4.66 (dd, *J* = 6.5, 6.5 Hz, 1 H), 5.89 (dd, *J* = 15.5, 6.5 Hz, 1 H), 5.96 (dddd, *J* = 15.5, 6.5, 6.5, 0.5 Hz, 1 H), 7.26–7.42 (m, 2 H), 7.46–7.48 (m, 1 H), 7.94–7.96 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.83, 26.89, 27.23, 34.01, 34.32, 35.07, 44.48, 44.52, 71.02, 85.51, 128.46, 128.95, 129.01, 129.14, 131.99, 133.28, 163.03 ppm.

***N*-[(*E*,2*S*,3*S*)-6-Chloro-3-hydroxy-1-phenylhex-4-en-2-yl]benzamide (7a):** 1 N HCl (14 mL, 14 mmol, 5 equiv.) was added to a stirred solution of allylic chloride **6a** (2.81 mmol, 1 equiv.) in THF (28 mL) and MeOH (28 mL) at room temp., and the reaction mixture was stirred for 12 h. Saturated aqueous $NaHCO_3$ (70 mL) was added, and stirring was continued for 3 h. The reaction mixture was extracted with EtOAc (4 × 50 mL), and the combined organic layers were washed with brine (50 mL), dried with $MgSO_4$, and concentrated in vacuo. Purification by silica gel chromatography (ethyl acetate/hexane = 1:1) gave alcohol **7a** in 91% yield; white solid. $[\alpha]_D^{20}$ = –61.2 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 3329, 1633, 1527, 1487, 1295 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.06 (m, 2 H), 4.01 (m, 2 H), 4.30 (m, 2 H), 5.83 (dd, *J* = 15.5, 5.5 Hz, 1 H), 5.89

(dddd, *J* = 15.5, 6.5, 6.5, 1 Hz, 1 H), 6.45 (d, *J* = 8 Hz, 1 H), 7.24–7.33 (m, 5 H), 7.39–7.43 (m, 2 H), 7.48–7.51 (m, 1 H), 7.66–7.68 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = 38.34, 44.89, 56.27, 72.06, 127.47, 127.63, 128.52, 129.32, 129.43, 129.99, 132.36, 135.05, 135.40, 138.53, 168.77 ppm. According to the procedure described above for the alcohol **7a**, allylic chlorides **6b**–**d** were converted into alcohols **7b**–**d**.

***N*-[(*E*,3*S*,4*S*)-7-Chloro-4-hydroxy-2-methylhept-5-en-3-yl]benzamide (7b):** 97% yield; white solid. $[\alpha]_D^{20}$ = –36.5 (*c* = 1.0, CHCl$_3$). IR (neat): ṽ = 3341, 1622, 1542, 1413, 1149 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 1.02 (d, *J* = 6.5 Hz, 3 H), 1.08 (d, *J* = 6.5 Hz, 3 H), 2.07 (m, 1 H), 3.82 (ddd, *J* = 9.5, 9.5, 3 Hz, 1 H), 4.01 (m, 2 H), 4.50 (m, 1 H), 5.85 (dd, *J* = 15, 5 Hz, 1 H), 5.92 (m, 1 H), 6.41 (d, *J* = 9.5 Hz, 1 H), 7.43–7.46 (m, 2 H), 7.50–7.53 (m, 1 H), 7.76–7.78 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = 19.95, 20.69, 30.46, 44.95, 59.97, 71.91, 127.61, 128.21, 129.34, 132.27, 135.28, 135.87, 168.90 ppm.

***N*-[(*E*,4*S*,5*S*)-8-Chloro-5-hydroxy-2-methyloct-6-en-4-yl]benzamide (7c):** 97% yield; white solid. $[\alpha]_D^{20}$ = –43.3 (*c* = 1.0, CHCl$_3$). IR (neat): ṽ = 3329, 2955, 1635, 1535, 1289 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 0.96 (m, *J* = 6.5 Hz, 6 H), 1.49 (m, 1 H), 1.60–1.73 (m, 2 H), 3.12 (s, 1 H), 4.02 (m, 2 H), 4.22–4.27 (m, 2 H), 5.83–5.93 (m, 2 H), 6.38 (d, *J* = 9 Hz, 1 H), 7.39–7.43 (m, 2 H), 7.47–7.51 (m, 1 H), 7.73–7.77 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = 22.84, 24.00, 25.73, 41.46, 45.03, 52.83, 74.30, 127.66, 128.49, 129.29, 132.30, 135.11, 135.40, 168.79 ppm.

***N*-[(*E*,2*S*,3*S*)-6-Chloro-1-cyclohexyl-3-hydroxyhex-4-en-2-yl]-benzamide (7d):** 85% yield; white solid. $[\alpha]_D^{20}$ = –49.0 (*c* = 1.0, CHCl$_3$). IR (neat): ṽ = 3326, 2921, 1632, 1536, 1488, 1447 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 0.88–0.91 (m, 1 H), 0.92–0.01 (m, 1 H), 1.13–1.23 (m, 3 H), 1.34–1.37 (m, 2 H), 1.54–1.70 (m, 5 H), 1.86–1.88 (m, 1 H), 3.03 (d, *J* = 4.5 Hz, 1 H), 3.99–4.08 (m, 2 H), 4.24–4.27 (m, 2 H), 5.83–5.91 (m, 2 H), 6.34 (d, *J* = 5.5 Hz, 1 H), 7.40–7.44 (m, 2 H), 7.48–7.51 (m, 1 H), 7.73–7.77 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = 26.82, 26.97, 27.17, 33.49, 34.60, 35.12, 39.94, 45.03, 52.19, 74.35, 127.66, 127.74, 128.50, 129.30, 129.39, 132.29, 135.16, 135.41, 168.74 ppm.

***N*-[(*E*,2*S*,3*S*)-3-(*tert*-Butyldimethylsilyloxy)-6-chloro-1-phenylhex-4-en-2-yl]benzamide (1a):** Imidazole (0.92 g, 13.46 mmol, 6 equiv.) and *tert*-butylchlorodimethylsilane (2.03 g, 13.46 mmol, 6 equiv.) were added to a stirred solution of alcohol **7a** (2.24 mmol, 1 equiv.) in DMF (25 mL) at room temp., and stirring was continued for 2 h. The reaction mixture was quenched with H$_2$O (100 mL) and extracted with EtOAc (5 × 20 mL). The combined organic layers were washed with brine, dried with MgSO$_4$, and concentrated in vacuo. Purification by silica gel chromatography (ethyl acetate/hexane = 1:8) gave silyl ether **1a** in 93% yield; white solid. $[\alpha]_D^{20}$ = –80.9 (*c* = 1.0, CHCl$_3$). IR (neat): ṽ = 3303, 2953, 2856, 1637, 1532 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 0.08 (s, 3 H), 0.15 (s, 3 H), 1.00 (s, 9 H), 2.93 (m, 2 H), 3.97 (m, 2 H), 4.33 (dd, *J* = 5.5, 1.5 Hz, 1 H), 4.40 (ddd, *J* = 11.5, 7.5, 2 Hz, 1 H), 5.76 (m, 2 H), 6.47 (d, *J* = 8.5 Hz, 1 H), 7.20–7.31 (m, 5 H), 7.41–7.51 (m, 3 H), 7.68–7.70 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = –4.05, –3.02, 18.91, 26.70, 38.47, 44.92, 56.06, 72.62, 127.27, 127.43, 128.44, 129.28, 129.35, 129.85, 132.16, 135.37, 138.69, 167.55 ppm. HRMS (FAB): calcd. for C$_{25}$H$_{35}$ClNO$_2$Si [M + H]$^+$ 444.2126; found 444.2117. According to the procedure described above for the allylic chloride **1a**, alcohols **7b**–**d** were converted into allylic chlorides **1b**–**d**.

***N*-[(*E*,3*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-7-chloro-2-methylhept-5-en-3-yl]benzamide (1b):** 94% yield; white solid. $[\alpha]_D^{20}$ = –39.1 (*c* = 1.0, CHCl$_3$). IR (neat): ṽ = 2955, 2929, 1654, 1513, 1485, 1254 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 0.08 (dd, *J* = 5.5, 5.5 Hz, 3 H), 0.12 (dd, *J* = 3, 3 Hz, 3 H), 0.95 (m, 9 H), 0.99 (d, *J* = 6.5 Hz, 3 H), 1.05 (d, *J* = 6.5 Hz, 3 H), 1.87 (m, 1 H), 3.79 (ddd, *J* = 9.5, 9.5, 1.5 Hz, 1 H), 3.96 (m, 2 H), 4.78 (dd, *J* = 5, 1.5 Hz, 1 H), 5.77 (m, 2 H), 6.47 (d, *J* = 9.5 Hz, 1 H), 7.43–7.47 (m, 2 H), 7.49–7.51 (m, 1 H), 7.74–7.76 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = –4.16, –2.91, 18.84, 20.39, 20.59, 26.66, 30.93, 45.07, 60.04, 72.24, 127.43, 127.97, 129.37, 132.10, 135.55, 136.10, 167.82 ppm. HRMS (FAB): calcd. for C$_{21}$H$_{35}$ClNO$_2$Si [M + H]$^+$ 396.2126; found 396.2149.

***N*-[(*E*,4*S*,5*S*)-5-(*tert*-Butyldimethylsilyloxy)-8-chloro-2-methyloct-6-en-4-yl]benzamide (1c):** 91% yield; white solid. $[\alpha]_D^{20}$ = –40.8 (*c* = 1.0, CHCl$_3$). IR (neat): ṽ = 2954, 2857, 1637, 1520, 1487, 1254 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 0.08 (s, 3 H), 0.12 (s, 3 H), 0.90–0.98 (m, 15 H), 1.46 (m, 2 H), 1.65 (m, 1 H), 3.99 (m, 2 H), 4.23 (dd, *J* = 3.5, 2.5 Hz, 1 H), 5.79 (m, 2 H), 6.23 (d, *J* = 9.5 Hz, 1 H), 7.42–7.45 (m, 2 H), 7.48–7.50 (m, 1 H), 7.73–7.75 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = –4.20, –3.40, 18.87, 23.02, 23.96, 25.62, 26.39, 26.55, 26.63, 41.91, 45.08, 52.58, 74.15, 127.44, 128.08, 129.32, 132.10, 135.45, 135.55, 167.59 ppm. HRMS (FAB): calcd. for C$_{22}$H$_{37}$ClNO$_2$Si [M + H]$^+$ 410.2282; found 410.2283.

***N*-[(*E*,2*S*,3*S*)-3-(*tert*-Butyldimethylsilyloxy)-6-chloro-1-cyclohexylhex-4-en-2-yl]benzamide (1d):** 96% yield; white solid. $[\alpha]_D^{20}$ = –52.3 (*c* = 1.0, CHCl$_3$). IR (neat): ṽ = 2925, 2853, 1636, 1532, 1487, 1252 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 0.08–0.12 (m, 6 H), 0.87–1.01 (m, 11 H), 1.15–1.23 (m, 4 H), 1.42–1.50 (m, 2 H), 1.62–1.70 (m, 4 H), 1.874 (m, 1 H), 3.99 (m, 2 H), 4.25–4.27 (m, 2 H), 5.79 (m, 2 H), 6.19 (d, *J* = 9 Hz, 1 H), 7.43–7.46 (m, 2 H), 7.49–7.50 (m, 1 H), 7.73–7.75 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = –4.19, –3.41, 18.87, 26.36, 26.55, 26.63, 26.88, 26.98, 27.22, 33.66, 34.61, 35.03, 40.27, 45.10, 51.88, 74.07, 127.44, 128.05, 129.32, 132.07, 135.54, 135.57, 167.52 ppm. HRMS (FAB): calcd. for C$_{25}$H$_{41}$ClNO$_2$Si [M + H]$^+$ 450.2595; found 450.2586.

General Procedure for the Preparation of (4*S*,5*R*,6*R*)-1,3-Oxazines (at 0 °C): NaH (60% in mineral oil, 32 mg, 0.79 mmol, 2 equiv.) and *n*Bu$_4$NI (146 mg, 0.40 mmol, 1 equiv.) were added to a stirred solution of silyl ether **1** (0.40 mmol, 1 equiv.) in dry THF (15 mL) at 0 °C. After 5 min, Pd(PPh$_3$)$_4$ (92 mg, 0.08 mmol, 0.2 equiv.) was added, and stirring was continued at the same temperature for 5 h. The reaction mixture was filtered through a pad of silica and then concentrated under reduced pressure to give the crude product. Purification of this material by silica gel chromatography (ethyl acetate/hexane = 1:30) gave mixture **2**.

(4*S*,5*R*,6*R*)-4-Benzyl-5-(*tert*-butyldimethylsilyloxy)-5,6-dihydro-2-phenyl-6-vinyl-4*H*-1,3-oxazine (*syn*-2a): 80% yield, *syn*/*anti* = 8.3:1; purification by flash column chromatography (ethyl acetate/hexane = 1:50) gave pure product as a colorless oil. $[\alpha]_D^{20}$ = –108.2 (*c* = 1.0, CHCl$_3$). IR (neat): ṽ = 2929, 2856, 1659, 1255, 1116 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 0.08–0.12 (m, 6 H), 0.87 (m, 9 H), 2.89 (m, 2 H), 3.81 (m, 1 H), 4.09 (dd, *J* = 2.5, 1.5 Hz, 1 H), 4.68 (ddd, *J* = 6, 1.5, 1.5 Hz, 1 H), 5.34 (ddd, *J* = 10.5, 1.5, 1.5 Hz, 1 H), 5.46 (ddd, *J* = 17, 1.5, 1.5 Hz, 1 H), 6.01 (ddd, *J* = 17, 10.5, 6 Hz, 1 H), 7.22–7.25 (m, 1 H), 7.32–7.41 (m, 7 H), 7.95–7.97 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$): δ = –2.92, –2.63, 19.04, 26.70, 40.36, 60.42, 68.93, 79.62, 118.27, 126.67, 127.98, 128.65, 128.81, 130.26, 130.80, 134.53, 135.83, 141.10, 154.20 ppm. HRMS (FAB): calcd. for C$_{25}$H$_{34}$NO$_2$Si [M + H]$^+$ 408.2359; found 408.2315.

(4*S*,5*R*,6*R*)-5-(*tert*-Butyldimethylsilyloxy)-5,6-dihydro-4-isopropyl-2-phenyl-6-vinyl-4*H*-1,3-oxazine (*syn*-2b): 73% yield, *syn*/*anti* = 13.4:1; purification by flash column chromatography (ethyl acetate/

hexane = 1:50) gave pure product as a colorless oil. $[\alpha]_D^{20}$ = –37.6 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2955, 2858, 1662, 1468, 1254, 1108 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 0.06 (dd, *J* = 2.5, 2.5 Hz, 6 H), 0.79 (m, 9 H), 1.01 (d, *J* = 6.5 Hz, 3 H), 1.25 (d, *J* = 6.5 Hz, 3 H), 1.83 (ddd, *J* = 10, 6.5, 6.5 Hz, 1 H), 3.00 (dd, *J* = 10, 2.5 Hz, 1 H), 4.16 (dd, *J* = 2.5, 1.5 Hz, 1 H), 4.63 (ddd, *J* = 6.5, 1.5, 1.5 Hz, 1 H), 5.34 (ddd, *J* = 10.5, 1.5, 1.5 Hz, 1 H), 5.47 (ddd, *J* = 17.5, 1.5, 1.5 Hz, 1 H), 6.01 (ddd, *J* = 17.5, 10.5, 6.5 Hz, 1 H), 7.33–7.40 (m, 3 H), 7.96–7.98 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = –2.87, –2.74, 19.18, 20.77, 21.04, 26.77, 29.75, 65.64, 67.01, 80.50, 118.40, 127.94, 128.53, 130.63, 134.83, 136.25, 154.10 ppm. HRMS (FAB): calcd. for $C_{21}H_{34}NO_2Si$ [M + H]$^+$ 360.2359; found 360.2356.

(4*S*,5*R*,6*R*)-5-(*tert*-Butyldimethylsilyloxy)-5,6-dihydro-4-isobutyl-2-phenyl-6-vinyl-4*H*-1,3-oxazine (*syn*-2c): 88% yield, *syn*/*anti* = 9.0:1; purification by flash column chromatography (ethyl acetate/hexane = 1:50) gave pure product as a colorless oil. $[\alpha]_D^{20}$ = –37.9 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2954, 2859, 2659, 1467, 1255, 1113 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 0.06 (s, 3 H), 0.07 (s, 3 H), 0.83 (s, 9 H), 0.97 (d, *J* = 7 Hz, 3 H), 1.00 (d, *J* = 7 Hz, 3 H), 1.36 (m, 1 H), 1.57 (m, 3 H), 2.08 (m, 1 H), 3.61 (m, 1 H), 3.92 (dd, *J* = 2.5, 1.5 Hz, 1 H), 4.68 (ddd, *J* = 6, 1.5, 1.5 Hz, 1 H), 5.31 (ddd, *J* = 10.5, 1.5, 1.5 Hz, 1 H), 5.44 (ddd, *J* = 17.5, 1.5, 1.5 Hz, 1 H), 5.99 (ddd, *J* = 17.5, 10.5, 6 Hz, 1 H), 7.33–7.39 (m, 3 H), 7.95–7.97 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = –2.97, –2.76, 19.00, 23.03, 24.12, 25.04, 26.71, 42.96, 56.52, 68.76, 79.98, 118.19, 127.95, 128.58, 130.69, 134.75, 136.09, 154.17 ppm. HRMS (EI): calcd. for $C_{22}H_{35}NO_2Si$ [M]$^+$ 373.2437; found 373.2421.

(4*S*,5*R*,6*R*)-5-(*tert*-Butyldimethylsilyloxy)-4-(cyclohexylmethyl)-5,6-dihydro-2-phenyl-6-vinyl-4*H*-1,3-oxazine (*syn*-2d): 89% yield, *syn*/*anti* = 14.0:1; purification by flash column chromatography (ethyl acetate/hexane = 1:50) gave pure product as a colorless oil. $[\alpha]_D^{20}$ = –44.5 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2925, 1659, 1447, 1254, 1155 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 0.06 (s, 6 H), 0.82 (s, 9 H), 0.88–1.05 (m, 3 H), 1.20–1.40 (m, 5 H), 1.53–1.56 (m, 1 H), 1.69–1.90 (m, 4 H), 3.65 (m, 1 H), 3.91 (dd, *J* = 2.5, 1.5 Hz, 1 H), 4.67 (ddd, *J* = 6.5, 1.5, 1.5 Hz, 1 H), 5.31 (ddd, *J* = 10.5, 1.5, 1.5 Hz, 1 H), 5.44 (ddd, *J* = 17.5, 1.5, 1.5 Hz, 1 H), 5.99 (ddd, *J* = 17.5, 10.5, 6.5 Hz, 1 H), 7.33–7.39 (m, 3 H), 7.94–7.96 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = –2.99, –2.72, 19.00, 26.71, 27.02, 27.16, 27.51, 33.82, 34.46, 34.82, 41.54, 55.70, 68.82, 79.97, 118.17, 127.96, 128.58, 130.69, 134.75, 136.09, 154.22 ppm. HRMS (EI): calcd. for $C_{25}H_{39}NO_2Si$ [M]$^+$ 413.2750; found 413.2762.

General Procedure for the Preparation of (4*S*,5*R*,6*S*)-1,3-Oxazines (at 40 °C): NaH (60% in mineral oil, 10 mg, 0.248 mmol, 2 equiv.) and *n*Bu_4NI (46 mg, 0.124 mmol, 1 equiv.) were added to a stirred solution of silyl ether **1** (0.124 mmol, 1 equiv.) in dry THF (5 mL) at room temp. After 5 min, $Pd(PPh_3)_4$ (29 mg, 0.025 mmol, 0.2 equiv.) was added, and stirring was continued at 40 °C for 12 h. The reaction mixture was filtered through a pad of silica and then concentrated under reduced pressure to give the crude product. Purification of this material by silica gel chromatography (ethyl acetate/hexane = 1:30) gave mixture **2**.

(4*S*,5*R*,6*S*)-4-Benzyl-5-(*tert*-butyldimethylsilyloxy)-5,6-dihydro-2-phenyl-6-vinyl-4*H*-1,3-oxazine (*anti*-2a): 68% yield, *syn*/*anti* = 1:15; purification by flash column chromatography (ethyl acetate/hexane = 1:50) gave pure product as a colorless oil. $[\alpha]_D^{20}$ = –116.3 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2928, 2856, 1658, 1493, 1257, 1116 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 0.10 (m, 6 H), 0.91 (m, 9 H), 2.90 (dd, *J* = 13.5, 8.5 Hz, 1 H), 3.06 (dd, *J* = 13.5, 6 Hz, 1 H), 3.75 (ddd, *J* = 8.5, 6, 3.5 Hz, 1 H), 3.82 (dd, *J* = 5, 3.5 Hz, 1 H), 4.68 (dddd, *J* = 5.5, 5.5, 1.5, 1.5 Hz, 1 H), 5.27 (ddd, *J* = 10.5, 1.5, 1.5 Hz, 1 H), 5.35 (ddd, *J* = 17.5, 1.5, 1.5 Hz, 1 H), 5.85 (ddd, *J* = 17.5, 10.5, 5.5 Hz, 1 H), 7.22–7.42 (m, 8 H), 7.96–7.97 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = –3.65, –3.59, 18.85, 26.51, 39.08, 56.41, 68.20, 78.64, 118.25, 126.76, 127.97, 128.68, 128.88, 130.27, 131.00, 134.41, 135.30, 140.45, 153.60 ppm. HRMS (EI): calcd. for $C_{25}H_{33}NO_2Si$ [M]$^+$ 407.2281; found 407.2278.

(4*S*,5*R*,6*S*)-5-(*tert*-Butyldimethylsilyloxy)-5,6-dihydro-4-isopropyl-2-phenyl-6-vinyl-4*H*-1,3-oxazine (*anti*-2b): 77% yield, *syn*/*anti* = 1:16; purification by flash column chromatography (ethyl acetate/hexane = 1:50) gave pure product as a colorless oil. $[\alpha]_D^{20}$ = –47.7 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2954, 2858, 1662, 1468, 1356, 1255, 1168, 1102 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 0.12 (m, 6 H), 0.86 (m, 9 H), 0.99 (d, *J* = 6.5 Hz, 3 H), 1.22 (d, *J* = 6.5 Hz, 3 H), 1.91 (m, *J* = 9, 6.5, 6.5, 6.5 Hz, 1 H), 2.87 (dd, *J* = 9, 2.5 Hz, 1 H), 4.01 (dd, *J* = 2.5, 2.5 Hz, 1 H), 4.78 (dddd, *J* = 4.5, 2.5, 2, 1 Hz, 1 H), 5.26 (ddd, *J* = 10.5, 1, 1 Hz, 1 H), 5.30 (ddd, *J* = 17.5, 2, 1 Hz, 1 H), 5.83 (ddd, *J* = 17.5, 10.5, 4.5 Hz, 1 H), 7.35–7.41 (m, 3 H), 7.99–8.01 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = –3.76, –3.59, 18.79, 20.45, 20.57, 26.39, 29.94, 59.20, 66.83, 80.01, 117.58, 127.89, 128.62, 130.72, 134.92, 135.36, 152.59 ppm. HRMS (EI): calcd. for $C_{21}H_{33}NO_2Si$ [M]$^+$ 359.2281; found 359.2280.

(4*S*,5*R*,6*S*)-5-(*tert*-Butyldimethylsilyloxy)-5,6-dihydro-4-isobutyl-2-phenyl-6-vinyl-4*H*-1,3-oxazine (*anti*-2c): 72% yield, *syn*/*anti* = 1:7.5; purification by flash column chromatography (ethyl acetate/hexane = 1:50) gave pure product as a colorless oil. $[\alpha]_D^{20}$ = –77.3 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2954, 2860, 1659, 1492, 1362, 1256, 1111 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 0.09 (m, 6 H), 0.88 (m, 9 H), 0.87 (d, *J* = 6.5 Hz, 3 H), 0.99 (d, *J* = 6.5 Hz, 3 H), 1.43 (m, 1 H), 1.61 (m, 1 H), 1.98 (m, 1 H), 3.59 (m, 1 H), 3.78 (dd, *J* = 5.5, 4.5 Hz, 1 H), 4.65 (dddd, *J* = 5.5, 5.5, 1.5, 1.5 Hz, 1 H), 5.31 (ddd, *J* = 10.5, 1.5, 1.5 Hz, 1 H), 5.40 (ddd, *J* = 17.5, 1.5, 1.5 Hz, 1 H), 5.91 (ddd, *J* = 17.5, 10.5, 5.5 Hz, 1 H), 7.34–7.43 (m, 3 H), 7.96 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = –3.84, –3.73, 18.76, 23.29, 24.18, 25.32, 26.43, 41.77, 52.98, 68.72, 78.37, 118.18, 127.93, 128.67, 130.87, 134.55, 135.72, 153.16 ppm. HRMS (EI): calcd. for $C_{22}H_{35}NO_2Si$ [M]$^+$ 373.2437; found 373.2440.

(4*S*,5*R*,6*S*)-5-(*tert*-Butyldimethylsilyloxy)-4-(cyclohexylmethyl)-5,6-dihydro-2-phenyl-6-vinyl-4*H*-1,3-oxazine (*anti*-2d): 73% yield, *syn*/*anti* = 1:8.5; purification by flash column chromatography (ethyl acetate/hexane = 1:50) gave pure product as a colorless oil. $[\alpha]_D^{20}$ = –84.6 (*c* = 1.0, $CHCl_3$). IR (neat): ṽ = 2926, 2853, 1658, 1448, 1256, 1116 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 0.08 (s, 6 H), 0.88 (s, 9 H), 0.88–1.05 (m, 3 H), 1.20–1.40 (m, 5 H), 1.53–1.56 (m, 1 H), 1.69–1.90 (m, 4 H), 3.61 (m, 1 H), 3.77 (dd, *J* = 5.5, 4 Hz, 1 H), 4.65 (dd, *J* = 5.5, 5 Hz, 1 H), 5.30 (ddd, *J* = 10.5, 1.5, 1.5 Hz, 1 H), 5.39 (ddd, *J* = 17.5, 1.5, 1.5 Hz, 1 H), 5.89 (ddd, *J* = 17.5, 10.5, 5 Hz, 1 H), 7.35–7.41 (m, 3 H), 7.94–7.97 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = –3.83, –3.68, 18.76, 26.44, 26.71, 27.16, 27.44, 34.06, 34.46, 34.88, 40.3652.30, 68.73, 78.33, 118.16, 127.93, 128.66, 130.86, 134.57, 135.71, 153.17 ppm. HRMS (EI): calcd. for $C_{25}H_{39}NO_2Si$ [M]$^+$ 413.2750; found 413.2747.

***N*-{(*S*)-1-[(4*R*,5*R*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl]-2-methylpropyl}benzamide (10):** 3 N HCl (0.49 mL, 1.47 mmol, 15 equiv.) was added to a stirred solution of oxazine ***syn*-2b** (35 mg, 0.097 mmol, 1 equiv.) in THF (1 mL) and MeOH (1 mL) at room temp. The reaction mixture was stirred for 12 h, saturated aqueous $NaHCO_3$ (5 mL) was added, and stirring was continued for 3 h. The reaction mixture was extracted with EtOAc (4 × 15 mL), and the combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, and concentrated in vacuo. Purification by silica gel chromatography (ethyl acetate/hexane = 1:2) gave alcohol **8**. Tetrabutylammonium fluoride (1 M solution in THF, 0.040 mL, 0.038 mmol, 1.1 equiv.) was added to a stirred solution of **8** (0.034 mmol, 1 equiv.) in dry THF (1.5 mL) at room temp. After 1 h, the reaction mixture was diluted with EtOAc (10 mL), washed with saturated aqueous NH_4Cl (2×50 mL), dried with $MgSO_4$, and concentrated in vacuo to give the crude diol. 2,2-Dimethoxypropane (0.033 mL, 0.272 mmol, 8 equiv.) and *p*-toluenesulfonic acid (0.65 mg, 0.0034 mmol, 0.1 equiv.) were added to a stirred solution of diol in dry acetone (0.5 mL) at room temp. After 1 h, the reaction mixture was concentrated in vacuo, diluted with H_2O (10 mL), extracted with Et_2O (3×10 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. Purification of this material by silica gel chromatography (ethyl acetate/hexane = 1:2) gave acetonide **10** in 70% yield (3 steps); colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00 (d, J = 7 Hz, 3 H), 1.02 (d, J = 7 Hz, 3 H), 1.42 (s, 3 H), 1.44 (s, 3 H), 1.94 (m, 1 H), 3.92 (dd, J = 8.5, 1 Hz, 1 H), 4.02 (ddd, J = 9.5, 7, 1 Hz, 1 H), 4.07 (dddd, J = 8.5, 6, 1, 1 Hz, 1 H), 5.30 (ddd, J = 9, 1, 1 Hz, 1 H), 5.48 (ddd, J = 17, 1, 1 Hz, 1 H), 5.83 (ddd, J = 17, 9, 6 Hz, 1 H), 6.52 (d, J = 9.5 Hz, 1 H), 7.44–7.48 (m, 2 H), 7.51–7.52 (m, 1 H), 7.80–7.82 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.99, 20.26, 27.75, 27.87, 32.71, 52.54, 80.46, 80.83, 109.85, 120.58, 127.48, 129.41, 132.28, 134.99, 135.12, 167.68 ppm.

***N*-{(*S*)-1-[(4*R*,5*S*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl]-2-methylpropyl}benzamide (11):** According to the procedure described above for **10**, oxazine ***anti*-2b** gave acetonide **11** in 20% yield; colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00 (m, 6 H), 1.42 (s, 3 H), 1.59 (s, 3 H), 1.96 (m, 1 H), 3.97 (ddd, J = 9, 6.5, 1 Hz, 1 H), 4.45 (dd, J = 7.5, 1 Hz, 1 H), 4.68 (dddd, J = 7.5, 7.5, 1.5, 1.5 Hz, 1 H), 5.19 (ddd, J = 10.5, 1.5, 1.5 Hz, 1 H), 5.30 (ddd, J = 17.5, 1.5, 1.5 Hz, 1 H), 5.79 (ddd, J = 17.5, 10.5, 7.5 Hz, 1 H), 6.56 (d, J = 9 Hz, 1 H), 7.42–7.51 (m, 3 H), 7.75–7.77 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.58, 20.15, 25.08, 27.89, 33.29, 53.56, 77.96, 80.08, 108.93, 119.57, 127.45, 129.32, 131.97, 134.18, 135.97, 167.26 ppm.

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