Oxazolidinones and 2,5-Dihydrofurans via Zinc-Catalyzed Regioselective Allenylation Reactions of L-α-Amino Aldehydes

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Disciplines
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Publication Details

This journal article is available at Research Online: https://ro.uow.edu.au/smhpapers/4823
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Abstract

The simultaneous control of diastereoselectivity and regioselectivity in Zn-catalyzed allenylation reactions of N-protected L-α-amino aldehydes is reported. A reversal in diastereoselectivity could be realized by variation of the α-amino aldehyde protecting groups. A range of 1-allenyl-2-amino alcohols were obtained with excellent regioselectivity and converted to oxazolidinones and dihydrofurans. Many of which could be isolated as single diastereoisomers and without significant erosion of ee, making this a practical catalytic synthesis of highly functionalized heterocycles.

Introduction

Allenyl and propargyl boronates have emerged as key reagents for catalyzed allenylation and propargylation reactions of carbonyls and imines, providing rapid synthesis of allenes and alkynes with pendant heteroatoms via C–C bond formation.1 Allenes are valuable intermediates for target-oriented synthesis and methodology development because they can undergo a vast array of transformations and have high levels of structural diversity.1e Allenes bearing pendant heteroatoms, such as N or O, are particularly important due to the ability of these heteroatoms to engage in cyclization reactions with the reactive allene moiety – typically under the catalysis of π-philic transition metals.2 Furthermore, a number of natural products and
pharmaceuticals feature allenes with pendant heteroatoms.\textsuperscript{3}

A powerful route to allenes with a pendant O has been developed by Fandrick \textit{et al.} who have demonstrated that Et$_2$Zn catalyzes the regioselective allenylation of various achiral aldehydes and ketones with allenylboronic acid pinacol ester \textbf{I} (Scheme 1a).\textsuperscript{4a} This seminal study indicated that this was a kinetically controlled process, where addition of a catalytically generated propargyl zinc intermediate to the carbonyl electrophile competes with equilibration of the propargyl and allenyl intermediates. They also demonstrated that a regiochemical switch to the more typical homopropargyl alcohols was possible when the reaction was run at room temperature and under thermodynamic control.\textsuperscript{4b} More recently, Kobayashi showed that a Zn(HMDS)$_2$-catalyst process with allenylboronic acid 2,2-dimethyl-1,3-propanediol ester \textbf{I'} could also give either the allenyl or homopropargyl alcohols from the same starting materials by using kinetic or thermodynamic reaction control, respectively (Scheme 1a).\textsuperscript{5} Despite these reports, methods to prepare allenes with multiple pendant heteroatoms are extremely rare\textsuperscript{6} and mostly limited to systems containing only oxygen, rather than both O and N; furthermore, the methods that do exist are not catalytic.\textsuperscript{7} Combining both O and N reactive elements in a single allenic substrate would allow the synthesis of highly functionalized heterocycles with multiple heteroatoms. However, the potential route to these compounds via catalytic allenylation of $\alpha$-amino aldehydes\textsuperscript{8} (\textbf{A}, Scheme 1b) has not been developed; although the preparation of propargyl amino alcohols by the stoichiometric addition of propargylzinc species to $\alpha$-amino aldehydes has been established.\textsuperscript{9} Such a method would be challenging due to the requirement for concurrent control of both regioselectivity and diastereoselectivity – something that has not been achieved to date. Herein, we report a simultaneous control of diastereoselectivity and
regioselectivity in the Et₂Zn-catalyzed allenylation reactions of chiral α-amino aldehydes with allenylboronic acid pinacol ester 1.

Scheme 1. (a) Previous methods for the preparing allenylcarbinols from allenylboronic reagents 1 and 1’ using zinc catalysts; (b) current study.

The resulting allenic products are direct precursors to 2,5-dihydrofurans with a pendant N (25, Scheme 1b) and allenyloxazolidinones (23, Scheme 1b), which are two key heterocycles in a diverse array of biologically active structures, fragrance compounds, antirheumatics and antidiabetics. Diastereoselective methods to prepare oxazolidinones with pendant unsaturated moieties are severely limited, and while the preparation of 2,5-dihydrofurans by Au-catalyzed cyclisation of allenes is
well known, the same method to 2,5-dihydrofurans with pendant N are unknown – the only other routes involve long non-general multi-step synthesis.\textsuperscript{13}

**Results and Discussion**

The L-alanine-derived N-Boc protected $\alpha$-amino aldehyde 2a\textsuperscript{8} was first chosen for investigation of these reactions using diethylzinc as a catalyst under the reaction conditions shown in Table 1. We chose to focus on diethylzinc as it is a commercially available and mild reagent unlikely to cause racemization of the $\alpha$-amino aldehyde starting materials. When the reaction of allenyl boronate 1 and the aldehyde 2a was conducted in toluene in the absence of Et\textsubscript{2}Zn (entry 1), a slow background reaction was observed to give only propargyl amino alcohol 16a, in low yield and with low diastereoselectivity. The addition of 5 mol% of the Et\textsubscript{2}Zn catalyst resulted in a more rapid reaction to give the allene 9a with almost complete control of allenyl to propargyl regioselectivity, but with modest syn diastereoselectivity (entry 2). Switching to the more polar solvent THF resulted in the reversal of regioselectivity to favour the propargyl product 16a, but with almost no diastereoselectivity (entry 3). The reaction also proceeded in CH\textsubscript{2}Cl\textsubscript{2} but with modest regioselectivity (entry 4). An increase in the amount of catalyst from 5 mol% to 10 mol% in toluene improved the yield significantly from 77\% (entry 2) to 92\% (entry 5), with moderate diastereoselectivity. In an attempt to improve the diastereoselectivity, the reaction was conducted at −40 °C (entry 6), but no reaction was observed.

At this point alternate protecting groups on the nitrogen were investigated in an attempt to further control the diastereoselectivity. The $N$-Ts and $N$-Fmoc alanals 3 and 4 (entries 7 and 8) did not undergo the desired allenylation/propargylation reaction, while $N$-Tr alanal 5 (entry 9) provided the corresponding 1-allenyl-2-amino
alcohol in high yield and regioselectivity – however, the diastereoselectivity was poor. After testing a range of singly $N$-protected $\alpha$-amino alanals, $N\,N$-diprotected $\alpha$-amino alanals were investigated to see if a switch in diastereoselectivity was possible by virtue of increased steric bulk at the nitrogen of these substrates (entries 10-12). The reaction of the $N$-Bn, $N$-Boc alanal 6a proved the most rewarding giving the allenyl product 13 with good regioselectivity (89:11) and high diastereoselectivity ($dr = 19:1\) \text{anti:syn}$).

**Table 1. Optimization of reaction conditions**

<table>
<thead>
<tr>
<th>Entry</th>
<th>NR1R2</th>
<th>Sol.</th>
<th>Cat. (mol %)</th>
<th>Yield(%)</th>
<th>(al:pr)$^c$</th>
<th>$dr^e$ (syn:anti)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NHBoc</td>
<td>PhMe</td>
<td>0</td>
<td>12 (0:100)</td>
<td>2.6:1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>NHBoc</td>
<td>PhMe</td>
<td>5</td>
<td>77 (97:3)</td>
<td>2.6:1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>NHBoc</td>
<td>THF</td>
<td>5</td>
<td>60 (5:95)</td>
<td>1.1:1</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>NHBoc</td>
<td>CH$_2$Cl$_2$</td>
<td>5</td>
<td>38 (71:29)</td>
<td>2:1</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>NHBoc</td>
<td>PhMe</td>
<td>10</td>
<td>92 (93:7)</td>
<td>2.6:1</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>NHBoc$^d$</td>
<td>PhMe</td>
<td>10</td>
<td>0$^g$</td>
<td>0$^g$</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>NHTs</td>
<td>PhMe</td>
<td>10</td>
<td>0$^g$</td>
<td>0$^g$</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>NHFmoc</td>
<td>PhMe</td>
<td>10</td>
<td>0$^g$</td>
<td>0$^g$</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>NHTs</td>
<td>PhMe</td>
<td>10</td>
<td>82 (84:16)</td>
<td>1.3:1</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>NBnBoc$^e$</td>
<td>PhMe</td>
<td>10</td>
<td>96 (89:11)</td>
<td>1:19$^h$</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>NBnTs$^e$</td>
<td>PhMe</td>
<td>10</td>
<td>54$^i$ (94:6)</td>
<td>1:1.5</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>NBnTs$^e$</td>
<td>PhMe</td>
<td>10</td>
<td>50$^i$ (94:6)</td>
<td>1:1.3</td>
<td></td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: 1 (1.10 equiv.), Et$_2$Zn, solvent, 0 °C, 18 h.  
$^b$Isolated yield of allene and propargyl products.  
$^c$Regioselectivity of determined by $^1$H NMR analysis of the crude reaction product – stereochemistry of propargyl products not determined.  
$^d$The reaction was carried out at -40 °C.  
$^e$Decomposition of SM.  
$^f$Recruitment of SM.  
$^g$1.3 equiv. of 1 was used.  
$^h$Determined by $^1$H NMR analysis of $N$-Boc deprotected crude RM. Lowering of the catalyst loading for this substrate resulted in incomplete conversion.  
$^i$Isolated yield for the major allene diastereoisomer.

The \textit{anti} and \textit{syn} configurations assigned to 9a and 13a, respectively, were based on $^1$H NMR analysis, including the nOe interactions between H4, H5 and the CH$_3$ group in the corresponding oxazolidinones 23a and 24 (Scheme 2) and the
magnitudes of $J_{4,5}$ couplings ($J_{4,5} = 6.0$ Hz for 23a and $J_{4,5} = 7.2$ Hz for 24) which were also consistent with these assignments. It is proposed that the syn diastereoisomer is likely formed via a Cram–chelate-like model, where interaction between the aldehyde and the N-H drives the direction of nucleophilic attack. (Scheme 2a). Conversely, switching to the aldehyde having a more steric bulky, doubly protected, nitrogen favors Felkin–Ahn control as H-bonding is no longer possible (Scheme 2b). That the $dr$ for the uncatalyzed reaction (Table 1, entry 1) is identical to the catalyzed provides further support for this H-bond model, rather than Zn playing a role in chelation.

**Scheme 2.** Determination of relative configuration of the allenyl products.

While only a moderate diastereoselectivity was observed for the allenylation of N-Boc protected $\alpha$-amino aldehyde 2a, the reactions are highly regioselective. Furthermore, the levels of diastereoselectivity observed in Table 2 are comparable to the recently reported cross-benzoin condensation using N-Boc protected $\alpha$-amino aldehydes. We found that base-induced conversion to the allenyl oxazolidinones 23 provides a
convenient method for producing regio- and diastereomerically enriched products (up to >98:2 for the majority of cases) after chromatographic purification for the removal of the minor diastereomer.

**Table 2. Reaction scope of 5-allenyl oxazolidinones**

<table>
<thead>
<tr>
<th>1-allenyl-2-aminoalcohols&lt;sup&gt;b,c&lt;/sup&gt;</th>
<th>5-allenyl oxazolidinone&lt;sup&gt;b,c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>9a, 92%, dr 2.6:1, 92:8 regiosel.</td>
<td>23a, 61%&lt;sup&gt;e&lt;/sup&gt; dr &gt;98:2</td>
</tr>
<tr>
<td></td>
<td>96% ee</td>
</tr>
<tr>
<td>9b, 81%, dr 5.2:1, 92:8 regiosel.</td>
<td>23b, 55%&lt;sup&gt;e&lt;/sup&gt; dr &gt;98:2</td>
</tr>
<tr>
<td></td>
<td>94% ee</td>
</tr>
<tr>
<td>9c, 81%, dr 5.7:1, 89:11 regiosel.</td>
<td>23c, 58%&lt;sup&gt;e&lt;/sup&gt; dr &gt;98:2</td>
</tr>
<tr>
<td></td>
<td>86% ee</td>
</tr>
<tr>
<td>9d, 88%, dr 9:1, 91:9 regiosel.</td>
<td>23d, 74%&lt;sup&gt;e&lt;/sup&gt; dr 4.3:1</td>
</tr>
<tr>
<td>9e, 80%, dr 2.5:1, 91:9 regiosel.</td>
<td>23e, 63% dr 3:1</td>
</tr>
<tr>
<td>9f, 78%, dr 2.5:1, 95:5 regiosel.</td>
<td>23f, 50%&lt;sup&gt;e&lt;/sup&gt; dr &gt;98:2</td>
</tr>
<tr>
<td></td>
<td>92% ee</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reactions conditions: (i) 1 (1.1 equiv.), Et<sub>2</sub>Zn (10 mol%), toluene, 0 °C, 18 h; (ii) NaH (2 equiv.), THF, r.t, 1.5 h.
<sup>b</sup>Isolated yield, with <i>dr</i> measured on purified oxazolidinone after chromatographic purification.
<sup>c</sup>Regioselectivity and <i>dr</i> estimated by <sup>1</sup>H NMR analysis of purified 9.
<sup>d</sup>Isolated yield of the single major diastereomer. 
<sup>e</sup><i>ee</i> was determined by <sup>1</sup>H NMR analysis of the resulting diastereomeric (S)-
camphorsulfonamide derivatives (see SI).

These structures are more convenient building blocks than the precursor N-protected amino-alcohols as their NMR spectra are more clearly defined due to the absence of rotamers and they have a rigid stereodefined oxazolidinone unit combined with a reactive allene moiety. This is the first example of oxazolidinones bearing a reactive C5 allenyl side chain along with the free NH, which suggests they should be powerful synthetic intermediates for the synthesis of biological active compounds. Therefore, the optimized reaction conditions for the Zn-catalyzed allenylation reactions were performed for other chiral N-Boc α-amino aldehydes having different aryl and aliphatic side chains, before conversion to the corresponding allenyl oxazolidinone (Table 2). These reactions afforded the syn 1-allenyl-2-amino alcohols 9a-9f with high regioselectivities and generally provided high yields (70-92%) and moderate to high diastereoselectivities (2.3:1–9:1 syn/anti). For the aliphatic R substituents, the dr improved as the size of the R group of 2 increased from Me (2a) to i-Pr (2d). The 1-allenyl-2-amino alcohol products underwent base-induced cyclisations to give 5-allenyloxazolidinones 23a-23f which could be isolated in yields of 50-74% – in the majority of cases (23a-c and 23f) these were obtained as single diastereomers, after separation of the major diasteromer using column chromatography, thus providing practical access to these intriguing heterocycles.

We next explored the substrate scope of the allenylation reaction of the N-Bn, N-Boc aldehydes 6. The NMR spectra for the direct allenylation products are complicated by the presence of a mixture of rotamers, diastereoisomers and regioisomers, therefore dihydrofurans 25 were targeted as the final desired products. Consequently, following allenylation of aldehydes 6a-g under the optimized conditions, a sequential Au(I)-catalyzed cyclization and N-Boc deprotection was
carried out on the crude reaction mixture to give dihydrofurans 25 in good three-step yields (Table 3). In three cases, the products (25a, 25d and 25f) could be obtained as single diastereoisomers after purification by column chromatography and the others in good to modest $dr$. The $dr$ as estimated by the $^1$H NMR of the crude dihydrofurans (25) is essentially the same as the purified material, except for 25f, which showed a $dr$ of 4.9:1 in the crude reaction mixture, indicating the minor diastereomer had been removed during purification. This method is advantageous for two reasons, firstly the dihydrofurans are medicinally important skeletons and secondly, the direct $N$-Boc deprotection of allene products 13 resulted in formation of an unstable product.$^{18}$ Despite the importance of these structures, we are unaware of any general methods to prepare 2,5-dihydrofurans with a pendant nitrogen atom – let alone in a stereodefined fashion. The $N$-Boc protected proline-derived amino aldehyde 6g performed well in the reaction to give 13g, and then the corresponding cyclized material 25g. The corresponding deprotected derivative proved unstable, which is consistent with previous reports.$^{19}$
All the α-amino aldehydes utilized in this study were enantiomerically enriched and obtained from naturally occurring L-α-amino acids and are generally known for their propensity to racemization. Therefore, the enantioretention of representative reactions from Tables 2 and Table 3 were investigated and gratifyingly, no erosion of enantiopurity was observed in any case. The ees of diastereomerically enriched oxazolidinones 23a-c and 23f were determined by preparation of their (S)-camphorsulfonyl derivatives according to the previously reported method (see SI). The ees of 23a (ee 96%) and 23c (ee 86%) were identical to those of their precursor aldehydes 2a (ee 96%) and 2c (ee 86%), which indicates little or no erosion of the
enantiomeric purities of the aldehydes during the reaction steps (aldehyde ee from chiral HPLC analysis of the corresponding alcohol, see SI). However, this method was not suitable for the 2,5-dihydrofuran products 25 due to instability of the corresponding camphorsulfonyl derivative. Therefore, the ee of the precursor aldehyde 6a (ee 91%) was determined by chiral HPLC (see SI), which was identical to that of its derived dihydrofuran 25a (ee 91%, from chiral HPLC analysis, see SI).

The proposed mechanism for these allenylation reactions is shown in Scheme 3 and is consistent with the proposal of Fandrick and co-workers. Transmetallation between 1 and Et₂Zn gives the reactive propargylic Zn species B, which under the kinetic control conditions of the reaction reacts in an Sₑ2’ fashion with the α-amino aldehyde under Felkin–Ahn or Cram–chelation-like control to give Zn alkoxide C. The reaction remains catalytic in Zn as the alkoxide can undergo B-to-Zn exchange with 1 to regenerate the propargyl zinc species B.

**Scheme 3.** Proposed catalytic cycle for the Zn-catalyzed allenylation reactions
It is also possible that Et₂Zn is regenerated by reaction of the alkoxide C with EtBpin generated in the initial transmetallation. Isomerisation of propargylic Zn species B to the thermodynamically more stable allene species D under our reaction conditions is clearly facilitated by more polar solvents, such as THF (entry 3 of Table 1).

In conclusion, we have developed the first examples of simultaneous control of diastereoselectivity and regioselectivity in Zn-catalyzed allenylation reactions of N-protected L-α-amino aldehydes. These reactions proceed with high regiochemical control to favor the allenic products. Felkin–Ahn control is observed in the presence of sterically hindered groups on nitrogen, while Cram–chelation like control is observed for singly protected α-amino aldehydes. Furthermore, the products of these allenylation reactions undergo intramolecular cyclization to obtain novel 5-allenyl oxazolidinones and 2,5-dihydrofurans. Many of these heterocyclic compounds could be obtained as single diastereomers in high ee after simple column chromatography, making this a practical method for preparing these highly functionalized and useful chiral scaffolds. Work is currently underway to investigate the reactivity of the allenyloxazolidinone products.

Experimental Section

General Methods. Commercial reagents were purchased and used as received without any purification. Dry reaction solvents were passed through activated alumina columns to obtain dryness before being stored under nitrogen over 4Å molecular sieves. All reactions using air/moisture sensitive reagents were performed in oven-dried glassware, under an atmosphere of nitrogen quipped with a stir bar. Reactions were monitored by thin-layer chromatography (TLC) on aluminum backed silica gel
sheets, visualizing with UV-light (254 nm) fluorescence quenching, followed by staining of the plates with potassium permanganate stain. Column chromatography used for compound purification was performed using pre-packed flash grade silica gel (40-75 nm) as the stationary phase. $^1$H NMR and $^{13}$C$\{^1$H$\}$ NMR spectra were recorded either at 300, 400 and 500 MHz $^1$H NMR or at 75, 100 and 125 MHz $^{13}$C NMR. All $^1$H NMR and $^{13}$C$\{^1$H$\}$ NMR were recorded in deuterated chloroform (CDCl$_3$) containing 0.1% (v/v) tetramethylsilane (TMS). Abbreviations used in the description of resonances are: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), broad (br) and multiplet (m). All coupling constants ($J$) were measured in hertz (Hz). NMR chemical shift abbreviations were reported in parts per millions (ppm) from tetramethylsilane (TMS) and were corrected to 0.00 ppm (TMS) for $^1$H NMR and 77.00 ppm (CDCl$_3$ centre line) for $^{13}$C NMR. The $\alpha$-amino amino methyl ester hydrochlorides were prepared from commercially available amino acids using previously reported literature procedures (citations to these compounds are provided in the experimental below).

**Synthesis of singly N-protected-amino Aldehydes**

The $N$-protected $\alpha$-amino aldehydes $2a$, $^{21}$a $2c$, $^{21}$b $2d$, $^{21}$c $2e$, $^{21}$d $3$, $^{21}$e $4$, $^{21}$f and $5$ are known and were prepared by the previously reported methods.

**Methyl (S)-tert-buty1(1-oxopentan-2-yl)carbamate (2b).**

*Methyl 2-((tert-butoxycarbonyl)amino)pentanoate S1.* To a solution of methyl 2-aminopentanoate hydrochloride$^{22}$a (1.00 g, 5.96 mmol) in dry dichloromethane (15 mL) at 0 °C, was added triethylamine ((0.94 mL, 6.55 mmol, 1.1 equiv.), followed by di-tert-butyl dicarbonate (1.56 g, 7.16 mmol, 1.2 equiv.). Stirring was continued for 1
h at 0 °C, and then overnight at room temperature. The reaction mixture was then quenched by the addition of saturated aqueous NaHCO$_3$(aq) solution and the separated organic layer washed with brine solution and dried over Na$_2$SO$_4$. Purification by flash column chromatography (EtOAc/hexane 3:7) yielded methyl 2-((tert-butoxycarbonyl)amino)pentanoate S1 as a colorless oil (1.29 g, 93% yield). $^1$H NMR matched that reported previously, but other characterization data has not been published so is included here.$^{23}$ $R_f$ (Et$_2$O/hexane 2:8) = 0.42. [$\alpha$]$^D_{D}^{22} = +84.6$ (c 2 CHCl$_3$). $^{13}$C($^1$H) NMR (125 MHz, CDCl$_3$) $\delta$ 13.5, 18.5, 28.1, 34.6, 52.0, 53.1, 79.5, 155.3, 173.4. IR ($\nu_{\max}$/cm$^{-1}$) 3370 (w), 2963 (m), 2934 (m), 1743 (s), 1713 (s), 1507 (s), 1365 (s), 1249 (s), 1159 (s), 1011 (m), 779 (m). HRMS (ESI-TOF) m/z calcd for C$_{11}$H$_{21}$NO$_4$Na [M + Na]$^+$ 254.1368, found 254.1361.

*Methyl (S)-tert-butyl(1-oxopentan-2-yl)carbamate (2b).* To a solution of methyl 2-((tert-butoxycarbonyl)amino)pentanoate S1 (0.19 g, 0.82 mmol) in dry toluene (2 mL) at −78 °C, was added dropwise diisobutylaluminum hydride (5.5 M in n-hexane, 0.30 mL, 1.64 mmol, 2 equiv.) over a period of 45 min. The mixture was stirred at the same temperature for 1.5 h, and then quenched by the addition of precooled methanol. The reaction mixture was allowed to warm to room temperature, ice (1 g) was added with heavy agitation, the mixture filtered and the filtrate was extracted with chloroform. The organic layer was washed with brine solution, dried over Na$_2$SO$_4$ and concentrated under reduced pressure to 2b as a colorless oil which was used without further purification (0.149 g, 91% yield). The data matched that previously reported.$^{24}$

(S)-tert-Butyl 3-(2-((tert-butoxycarbonyl)amino)-3-oxopropyl)-1H-indole-1-carboxylate (2f).
tert-Butyl 3-(2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)-1H-indole-1-carboxylate S2. Triethylamine (0.56 mL, 3.92 mmol, 1.0 equiv.) was added dropwise to a stirred solution of methyl tryptophanate hydrochloride\textsuperscript{22b} (1.00 g, 3.92 mmol) in THF (15 mL) at 0 °C. Then, di-tert-butyl dicarbonate (1.71 g, 7.85 mmol, 2.0 equiv.) and 4-(dimethylamino)pyridine (0.72 g, 5.88 mmol, 1.5 equiv.) were added and the mixture was stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure, and the tert-butyl 3-(2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)-1H-indole-1-carboxylate S2 was obtained after flash column chromatography (EtOAc/hexane 3:7). Colorless oil (1.59 g, 97%). The data recorded matched that previously reported.\textsuperscript{25}

(S)-tert-Butyl 3-(2-((tert-butoxycarbonyl)amino)-3-oxopropyl)-1H-indole-1-carboxylate (2f). The title compound 2f was obtained following the same procedure used for 2b with tert-butyl 3-(2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)-1H-indole-1-carboxylate S2 (0.11 g, 0.26 mmol) and diisobutylaluminum hydride (5.7 M in n-hexane, 0.10 mL, 0.57 mmol, 2.2 equiv.) in toluene (1 mL). Colorless gummy oil (0.064 g, 99% yield). [α]_D\textsuperscript{22} = +53.5 (c 3.2 CHCl\textsubscript{3}). \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) δ 1.44 (s, 9H, C(C\textsubscript{3}H\textsubscript{3})), 1.66 (s, 9H, C(C\textsubscript{3}H\textsubscript{3})), 3.22 (br s, 2H, CH\textsubscript{2}Ph), 4.48 (br s, 1H, CH), 5.22 (br s, 1H, NH), 7.25 (br s, 1H, CH\textsubscript{Ar}), 7.32 (br s, 1H, CH\textsubscript{Ar}), 7.43 (br s, 1H, CH\textsubscript{Ar}), 7.54 (br s, 1H, CH\textsubscript{Ar}), 8.13 (br s, 1H, CH\textsubscript{Ar}), 9.65 (s, 1H, CHO). \textsuperscript{13}C{\textsuperscript{1}H} NMR (125 MHz, CDCl\textsubscript{3}) δ 25.0, 28.2, 28.3, 59.6, 80.2, 83.8, 114.8, 115.3, 119.0, 122.7, 124.2, 124.7, 130.2, 135.5, 149.5, 155.4, 199.5. IR (\nu_{\text{max}}/\text{cm}^{-1}) 3371 (w), 2979 (m), 2361 (w), 1730 (s), 1700 (s), 1507 (s), 1452 (s), 1367 (s), 1253 (s), 1154 (s), 1086 (s), 856 (m), 766 (s), 744 (s). HRMS (ESI-TOF) m/z calcd for C\textsubscript{21}H\textsubscript{28}N\textsubscript{2}O\textsubscript{5}Na [M + Na]\textsuperscript{+} 411.1896, found 411.1878.
Preparation of doubly protected α-amino esters and aldehydes

The  N-Bn,N-Boc α-amino aldehyde 6e and the N-Boc α-amino proinal 6g, N-Bn,N-Ts α-amino alaninal 7 and N,N-dibenzyl-α-amino alaninal 8 are known and were prepared by the previously reported methods. The remaining  N-Bn,N-Boc α-amino aldehydes were prepared as described below. The starting materials methyl tosyl-L-alaninate, (S)-tert-butyl benzyl(1-hydroxypropan-2-yl)carbamate, (S)-methyl N-benzyl valinate and (S)-2-(benzylamino)-3-methylbutan-1-ol were prepared as previously described.

**tert-Butyl benzyl(1-oxopropan-2-yl)carbamate 6a.**

To a stirred solution of tert-butyl benzyl(1-hydroxypropan-2-yl)carbamate (0.42 g, 1.58 mmol) in CH₂Cl₂ (30 mL) at 0 °C, was added saturated aqueous NaHCO₃ solution (15 mL), KBr (0.18 g, 1.58 mmol, 1.0 equiv.) and TEMPO (12.35 mg, 0.079 mmol, 0.05 equiv.). NaOCl (3.79 mL, 1.89 mmol, 1.2 equiv.) was then added with a syringe pump over 30 min. The reaction was stirred for another 15 min at 0 °C. Then, the reaction mixture was quenched with saturated aqueous Na₂S₂O₃ solution (15 mL) and extracted into CH₂Cl₂ (3×10 mL). The combined organic layers were dried (Na₂SO₄) and concentrated under reduced pressure to afford the aldehyde 6a, which was utilized for the next step without purification. Colorless oil (0.38 g, 91%). The ee was determined by chiral HPLC analysis of the corresponding alcohol (obtained by NaBH₄ reduction of a small quantity of the unpurified aldehyde) using a Phenomenex Lux i-Cellulose-5 column; hexane/isopropanol (95:5); flow rate = 0.5 mL/min; 210 nm; tmajor = 23.29 min, tminor = 25.15 min, 91% ee. The data matches that previously reported.
(S)-

Methyl 2-(benzyl(tert-butoxycarbonyl)amino)pentanoate S4. Triethylamine (2.58 mL, 9.02 mmol, 2.0 equiv.) was added dropwise to a stirred solution of S3 (1.00 g, 4.51 mmol) and di-tert-butyl dicarbonate (Boc$_2$O, 1.47 g, 6.77 mmol, 1.5 equiv.) in dry dichloromethane (10 mL), and the reaction mixture was stirred for 24 h at room temperature. The reaction was washed with aqueous solution of HCl (1M) (15 mL), dried (Na$_2$SO$_4$), and concentrated under reduced pressure. Purification was carried out by flash column chromatography (Et$_2$O/hexane 1:9) to yield the N-Bn,N-Boc $\alpha$-amino ester S6. Colorless oil (0.89 g, 62%). $R_f$ (Et$_2$O/hexane 1:9) = 0.23. $\left[\alpha\right]_{D}^{22} = -50.4$ (c 5.5 CHCl$_3$). $^{13}$C{$_1$H} NMR (125 MHz, CDCl$_3$) $\delta$ 13.8, 19.0, 35.7, 51.5, 52.1, 60.5, 126.9, 128.2, 128.3, 139.9, 176.0. IR (v$_{\text{max}}$/cm$^{-1}$) 3735 (m), 3031 (w), 2957 (m), 1734 (s), 1456 (m), 1339 (m), 1267 (m), 976 (m), 732 (m), 698 (s). HRMS (ESI-TOF) m/z calcd for C$_{13}$H$_{20}$NO$_2$ [M + H]$^+$ 222.1494, found 222.1492.
9.5 CHCl₃. **¹H NMR** (300 MHz, CDCl₃) (mixture of rotamers) δ 0.79 (br s, 3H, CH₃), 1.24 (br s, 2H, CH₂), 1.40 (br s, 4.2H, C(CH₃)₃), 1.45 (br s, 4.8H, C(CH₂)₃), 1.62-1.75 (m, 1H, CH), 1.84-1.94 (m, 1H, CH), 3.55 (s, 3H, CH₃), 3.90-4.80 (m, 3H, CH₂Ph, CH), 7.19-7.28 (m, 5H, 5CH₃Ar). **¹³C{¹H} NMR** (75 MHz, CDCl₃) (mixture of rotamers, minor rotamer indicated by asterisk) δ 13.5, 19.5, 28.1, 31.6, 32.3*, 32.4, 49.4, 50.7*, 51.5, 58.5, 59.1*, 80.2, 126.8, 127.1, 128.0, 128.3, 138.0, 138.9*, 155.6, 172.1. **IR** (νmax/cm⁻¹) 3031 (w), 2961 (m), 2875 (w), 1739 (s), 1700 (s), 1452 (s), 1319 (m), 1248 (m), 1163 (m), 979 (m), 862 (m), 734 (m), 699 (s). **HRMS** (ESI-TOF) m/z calcd for C₁₈H₂₇NO₄Na [M + Na⁺] 344.1838, found 344.1833.

**tert-Butyl benzyl(1-hydroxypentan-2-yl)carbamate S5.** To a solution of lithium aluminum hydride (1 M solution in THF, 4.98 mL, 4.98 mmol, 2.0 equiv.) at 0 °C, was added dropwise methyl 2-(benzyl(tert-butoxycarbonyl)amino) pentanoate S4 (0.80 g, 2.49 mmol) in THF (3 mL) and the mixture was stirred at the same temperature for 30 min. The reaction was quenched with water (1 mL), filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (EtOAc/hexane 4:6) to obtain the corresponding α-amino alcohol product S5 as a colorless oil (0.60 g, 82%). **Rf** (EtOAc/hexane 4:6) = 0.61. [α]₂₂° = +16.3 (c 4.6 CHCl₃). **¹H NMR** (500 MHz, CDCl₃) (mixture of rotamers) δ 0.84 (br s, 3H, CH₃), 1.26 (br s, 2H, CH₂), 1.37 (br s, 7H, C(CH₃)₃, CH), 1.49 (br s, 4H, C(CH₃)₃, CH), 3.40-3.60 (m, 3H), 3.84-3.86 (m, 1H, CH), 4.21-4.70 (m, 2H, CH₂Ph), 7.21-7.27 (m, 5H, 5CH₃Ar). **¹³C{¹H} NMR** (125 MHz, CDCl₃) (mixture of rotamers, minor rotamer indicated by asterisk) δ 13.9, 19.7, 28.3, 30.9, 31.7*, 48.2*, 49.3, 59.2, 64.1, 80.1, 126.9, 127.6, 128.3, 139.6, 156.9. **IR** (νmax/cm⁻¹) 3446 (m), 2959 (m), 2930 (m), 2873 (m), 1665 (s), 1465 (m), 1410 (s), 1341 (m), 1243 (m), 1166 (s), 1053 (w), 862 (m), 734 (m), 699 (s).
tert-Butyl benzyl(1-oxopentan-2-yl)carbamate 6b. Swern oxidation of methyl tert-butyl benzyl(1-hydroxypentan-2-yl)carbamate S5 (0.59 g, 2.01 mmol) was carried out with oxalyl chloride (0.37 mL, 4.02 mmol, 2 equiv.), DMSO (0.61 mL, 8.04 mmol, 4 equiv.) and Et3N 4.56 mL, 32.17 mmol, 16 equiv.) in CH2Cl2 (5 mL) at −78 °C. The reaction mixture was quenched with saturated aqueous NaHCO3 solution (5 mL) and extracted into CH2Cl2 (3×3 mL). The combined organic layers were washed with brine solution (10 mL), dried (Na2SO4) and concentrated under reduced pressure to yield 6b as a colorless oil (0.50 g, 85%), which was used in the allenylation reaction without further purification. (Caution! This reaction is carried out at −78 °C as it has been reported that oxalyl chloride and dimethyl sulfoxide can react explosively at room temperature. Furthermore, this procedure should be carried out in a fumehood since a dimethyl sulfide is an odorous by-product of the reaction).32

Rf (EtOAc/hexane 1:9) = 0.43. [α]D22 = −92.3 (c 7.0 CHCl3). 1H NMR (300 MHz, CDCl3) (mixture of rotamers) δ 0.89 (t, 3H, J = 7.2 Hz, CH3), 1.34-1.41 (m, 2H, CH2), 1.45 (br s, 9H, C(CH3)3), 1.49-1.80 (m, 1H, CH), 1.89-1.99 (m, 1H, CH), 3.45 (br s, 0.6H, CH), 3.76 (br s, 0.4H, CH), 4.11-4.22 (m, 1H, CPh), 4.70 (br d, 0.4H, J = 15.0 Hz, CPh), 4.98 (br d, 0.6H, J = 15.0 Hz, CPh), 7.26-7.35 (m, 5H, 5CHAr), 9.35 (br s, 0.6H, CHO), 9.44 (br s, 0.4H, CHO). 13C{1H} NMR (75 MHz, CDCl3) (mixture of rotamers, minor rotamer indicated by asterisk) δ 13.8, 19.5, 28.1, 29.2*, 30.4, 51.4*, 51.8, 65.5, 80.9*, 81.3, 127.6, 128.3, 128.6, 137.7, 138.1*, 155.1, 199.5. IR (νmax/cm−1) 2965 (m), 2933 (m), 2876 (w), 1739 (s), 1692 (s), 1452 (s), 1405 (s), 1365 (s), 1249 (s), 1180 (s), 1002 (m), 864 (m), 735 (s), 699 (s). HRMS (ESI-TOF) m/z calcd for C17H27NO3Na [M + Na]+ 314.1732, found 314.1741.
**tert-Butyl benzyl(4-methyl-1-oxopentan-2-yl)carbamate (6c)**

*Methyl N-benzyl leucinate S6.* To a stirred suspension of L-methyl leucinate hydrochloride\(^{33}\) (1.0 g, 5.50 mmol) and benzyl bromide (0.7 mL, 6.05 mmol, 1.1 equiv.) in acetonitrile (20 mL), was added potassium carbonate (1.52 g, 11 mmol, 2 equiv.) and the mixture was stirred overnight at room temperature. The reaction mixture was washed with saturated aqueous NH\(_4\)Cl solution (20 mL) and water (20 mL), dried (MgSO\(_4\)), concentrated under reduced pressure and purified by flash column chromatography (Et\(_2\)O/hexane 1:9) to obtain the N-benzylated product S6. Light yellow oil (0.996 g, 77%). Data matches that reported previously.\(^{34}\)

*Methyl N-benzyl-N-(tert-butoxycarbonyl) leucinate S7.* Triethylamine (0.81 mL, 2.75 mmol, 1.1 equiv.) was added dropwise to a stirred solution of S6 (1.00 g, 4.51 mmol) and di-tert-butyl dicarbonate (Boc\(_2\)O, 0.67 g, 3.1 mmol, 1.24 equiv.) in dry dichloromethane (5 mL), and the reaction mixture was stirred for 24 h at room temperature. The reaction was washed with aqueous solution of HCl (1M) (5 mL), dried (Na\(_2\)SO\(_4\)), and concentrated under reduced pressure. Purification was carried out by flash column chromatography (Et\(_2\)O/hexane 1:9) to yield the N-Bn,N-Boc \(\alpha\)-amino ester S7. Colorless oil (0.59 g, 70%). Data matches that previously reported.\(^{35}\)

*tert-Butyl benzyl(4-methyl-1-oxopentan-2-yl)carbamate 6c.* To a solution of S9 (0.58 g, 1.74 mmol) in dry diethyl ether (3 mL) at \(-78^\circ\)C, was added dropwise diisobutylaluminum hydride (5.0 M in \(n\)-hexane, 0.70 mL, 3.49 mmol, 2 equiv.) over 45 min. The mixture was stirred at the same temperature for 1 h, and was quenched with methanol (1 mL). The reaction mixture was allowed to warm to room temperature, followed by adding water (2 mL). The crude mixture was filtered through a sintered glass funnel and the filtrate was washed with brine (20 mL). The
organic layer was dried (Na$_2$SO$_4$) and concentrated under reduced pressure to yield the desired aldehyde. Colorless oil (0.35 g, 65%). Data matches that previously reported.$^{14d}$

**tert-Butyl benzyl(3-methyl-1-oxobutan-2-yl)carbamate (6d)**

(S)-*Methyl N-benzyl-N-(tert-butoxycarbonyl) valinate S8. Triethylamine (3.32 mL, 11.56 mmol, 2 equiv.) was added dropwise to a stirred solution of (S)-methyl *N*-benzyl valinate$^{31a}$ (1.28 g, 5.78 mmol) and di-*tert*-butyl dicarbonate (Boc$_2$O, 2.14 g, 9.82 mmol, 1.7 equiv.) in dry dichloromethane (15 mL), and the reaction mixture was stirred for 24 h at room temperature. The reaction was washed with aqueous solution of HCl (1M) (15 mL), dried (Na$_2$SO$_4$), and concentrated under reduced pressure. Purification was carried out by flash column chromatography (Et$_2$O/hexane 1:9) to yield the *N*-Bn,*N*-Boc α-amino ester S8. Colorless oil (1.18 g, 63%). Data matches that previously reported.$^{31b}$ S8 was then converted into (S)-2-(benzylamino)-3-methylbutan-1-ol as previously reported for use in the next step.$^{31b}$

(S)-*tert*-Butylbenzyl(3-methyl-1-oxobutan-2-yl)carbamate 6d. Swern oxidation of (S)-2-(Benzyllamino)-3-methylbutan-1-ol$^{31b}$ (0.73 g, 2.48 mmol) was carried out with oxalyl chloride (0.46 mL, 4.96 mmol, 2 equiv.), DMSO (0.75 mL, 9.94 mmol, 4 equiv.) and Et$_3$N (5.63 mL, 39.68 mmol, 16 equiv.) in CH$_2$Cl$_2$ (5 mL) at −78 °C. The reaction mixture was quenched with saturated aqueous NaHCO$_3$ solution (5 mL) and extracted into CH$_2$Cl$_2$ (3×3 mL). The combined organic layers were washed with brine solution (10 mL), dried (Na$_2$SO$_4$) and concentrated under reduced pressure to yield 6d as a colorless oil (0.558 g, 77%), which was used in the allenylation reaction without further purification. Data matches that reported previously.$^{31b}$
(S)-tert-Butyl 3-(2-(benzyl(tert-butoxycarbonyl)amino)-3-oxopropyl)-1H-indole-1-carboxylate (6f)

Methyl benzyl-L-tryptophanate S9. Methyl tryptophan hydrochloride22b (3.60 g, 14.13 mmol) was neutralized into the free base by dissolving in diethyl ether (20 mL) followed by treating with saturated aqueous K₂CO₃ solution (20 mL). The organic layer was dried (Na₂SO₄) and concentrated under reduced pressure to obtain a light yellow oil. To a stirred suspension of neutralized tryptophan methyl ester and MgSO₄ (2.70 g) in dichloromethane (40 mL), was added benzaldehyde (1.43 mL, 14.13 mmol, 1 equiv.) and the mixture was stirred for 5 h at room temperature. The resulting imine compound was dissolved in dry methanol (30 mL) and NaBH₄ (0.58 g, 15.54 mmol, 1.1 equiv.) was added slowly at 0 °C. The solvent was evaporated after 1 h at 0 °C. Then the mixture was washed by NH₄OH (5%, 20 mL), extracted by ethyl acetate and dried (Na₂SO₄). Methyl benzyl-L-tryptophanate S9 was obtained after flash column chromatography (EtOAc/hexane 2:8) as a colorless gummy oil (3.12 g, 72%). Data matches that reported previously.22b

Methyl Nα-benzyl-Nα-(tert-butoxycarbonyl)-L-tryptophanate S10. Triethylamine (2.85 mL, 9.92 mmol, 2 equiv.) was added dropwise to a stirred solution of methyl benzyl-L-tryptophanate S10 (1.53 g, 4.96 mmol) and di-tert-butyl dicarbonate (1.02 g, 4.71 mmol, 0.95 equiv.) in dry dichloromethane (20 mL), and was stirred for 24 h at room temperature. The crude reaction mixture was concentrated under reduced pressure. Then title compound S10 was obtained after flash column chromatography (EtOAc/hexane 2:8). Colorless gummy oil (1.37 g, 67%). Data matches that reported previously.22b

tert-Butyl (S)-3-(2-(benzyl(tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)-1H-indole-1-carboxylate S11. To a stirred solution of methyl Nα-benzyl-
N\textsuperscript{\textalpha}-(tert-butoxycarbonyl)-L-tryptophanate S\textsc{10} (1.07 g, 2.62 mmol) and di-tert-butyl dicarbonate (0.85 g, 3.93 mmol, 1.5 equiv.) in dichloromethane (15 mL), was added 4-(dimethylamino)pyridine (0.063 g, 0.52 mmol, 0.2 equiv.) and the mixture was stirred overnight at room temperature. The reaction mixture was diluted with EtOAc (10 mL) and washed with water (30 mL) and saturated aqueous NaHCO\textsubscript{3} solution (30 mL) and brine (30 mL). The organic layer was dried (Na\textsubscript{2}SO\textsubscript{4}) and the filtrate was concentrated under reduced pressure. The title compound S\textsc{11} was obtained after flash column chromatography (EtOAc/hexane 2:9) as a colorless gummy oil (1.15 g, 86%).

R\textsubscript{f} (EtOAc/hexane 2:9) = 0.48. [\alpha]\textsuperscript{22}\textsubscript{D} = −67.2 (c 1.0 CHCl\textsubscript{3}). \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) (mixture of rotamers) \(\delta\) 1.48 (s, 9H, 3CH\textsubscript{3}), 1.65 (s, 9H, 3CH\textsubscript{3}), 3.10-3.39 (m, 2H, CH\textsubscript{2}), 3.62 (s, 3H, CH\textsubscript{3}), 4.15-4.39 (m, 3H, CH\textsubscript{2}, CH\textsubscript{3}), 7.01-7.42 (m, 9H, 9CH\textsubscript{Ar}), 8.11 (br d, 1H, J = 6.9 Hz, CH\textsubscript{Ar}). \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) (mixture of rotamers, minor rotamer indicated by asterisk) \(\delta\) 24.9*, 25.9, 28.2*, 28.3, 51.8*, 52.0, 59.6, 59.8*, 80.5*, 80.8, 83.2*, 83.4, 115.2, 115.3*, 116.5, 116.7*, 118.5, 118.7, 118.9*, 122.4, 124.00*, 124.09, 124.4, 124.3*, 126.9, 127.0, 127.1*, 127.6*, 127.9, 128.1*, 128.3, 128.5, 130.2*, 130.5, 135.4, 137.2, 137.6*, 149.5, 155.2, 171.4, 174.9*. IR (\(\nu\)\textsubscript{max}/cm\textsuperscript{-1}) = 2976 (m), 2931 (m), 2357 (w), 2167 (w), 1732 (s), 1695 (s), 1452 (s), 1365 (s), 1253 (s), 1155 (s), 1083 (s), 1016 (m), 858 (m), 742 (s), 698 (s). HRMS (ESI) m/z calcd for C\textsubscript{29}H\textsubscript{36}N\textsubscript{2}O\textsubscript{6}Na [M + Na]\textsuperscript{+} 531.2471, found 531.2492.

tert-Butyl (S)-3-(2-(N-benzylformamido)-3-methoxy-3-oxopropyl)-1H-indole-1-carboxylate \textsc{6f}. To a solution of tert-butyl 3-(2-(benzyl(tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)-1H-indole-1-carboxylate S\textsc{11} (0.55 g, 1.08 mmol) in diethyl ether (3 mL) at \(-78\) °C, was added dropwise diisobutylaluminum hydride (5.4 M in n-hexane, 0.40 mL, 2.16 mmol, 2 equiv.). The mixture was stirred at the same temperature for 1 h, and was quenched with methanol
(1 mL). The reaction mixture was allowed to warm to room temperature, followed by adding water (2 mL). The crude mixture was filtered and the filtrate was washed with brine solution (20 mL). The organic layer was dried (Na$_2$SO$_4$) and concentrated under reduced pressure to yield the desired aldehyde 6f. Light orange oil (0.398 g, 77%). $R_f$ (EtOAc/hexane 2:8) = 0.63. $\left[\alpha\right]_D^{22} = -113.5$ (c 9.8 CHCl$_3$). $^1$H NMR (500 MHz, CDCl$_3$) (mixture of rotamers) $\delta$ 1.49 (s, 9H, C(CH$_3$)$_3$), 1.67 (s, 9H, C(CH$_3$)$_3$), 3.04-3.09 (m, 0.5H, CH), 3.29-3.31 (m, 0.5H, CH), 3.37-3.42 (m, 1H, CH), 3.52 (t, 1H, $J =$ 16.0 Hz, CH), 3.76-3.77 (m, 1H, CHPh), 4.50 (d, 0.5H, $J =$ 15.0 Hz, CHPh), 4.76 (d, 0.5H, $J =$ 15.0 Hz, CHPh), 7.00 (br s, 2H, 2CH$_2_Ar$), 7.19-7.24 (m, 4H, 4CH$_2_Ar$), 7.31-7.41 (m, 3H, 3CH$_2_Ar$), 8.16 (br s, 1H, CH$_2_Ar$), 9.42 (s, 0.5H, CHO), 9.53 (0.5H, CHO). $^{13}$C{$^1$H} NMR (125 MHz, CDCl$_3$) (mixture of rotamers, minor rotamer indicated by asterisk) $\delta$ 22.7, 23.8*, 28.2, 28.3*, 52.0, 52.7*, 65.3, 66.0*, 81.2*, 81.8, 83.5*, 83.6, 115.4*, 115.5, 116.4, 116.7*, 118.5, 118.7*, 122.64, 122.69*, 124.2*, 124.3*, 124.5, 124.6, 127.6*, 127.75, 127.78*, 128.4, 128.63, 128.65*, 130.1, 130.4*, 135.6, 137.3, 137.5*, 149.5, 154.8, 155.3*, 198.6, 199.0*. IR ($\nu_{max}$/cm$^{-1}$) 2978 (m), 2814 (w), 2364 (w), 2163 (w), 1730 (s), 1733 (s), 1683 (s), 1452 (s), 1365 (s), 1308 (m), 1251 (s), 1154 (s), 1085 (s), 976 (m), 856 (s), 743 (s), 700 (s). HRMS (ESI-TOF) $m/z$ calcd for C$_{29}$H$_{33}$N$_2$O$_5$ [M − H]$^+$ 477.2389, found 477.2382.

(S)-Methyl N-benzyl-N-tosyl alaninate S12. The aldehyde 8 was prepared as previously reported$^{29}$ but a modified synthesis of the ester starting material required for its synthesis was employed. Potassium carbonate (2.37 g, 17.32 mmol, 2 equiv.) was added to a stirred solution of methyl tosyl-$L$-alaninate$^{21e}$ (2.23 g, 8.66 mmol) and benzyl bromide (1.50 mL, 13.00 mmol, 1.5 equiv.) in acetonitrile (30 mL), and was stirred overnight at room temperature. The reaction mixture was washed with
saturated aqueous NH₄Cl solution (50 mL) and water (50 mL), dried (MgSO₄), concentrated under reduced pressure and purified by flash column chromatography (EtOAc/hexane 3:7) to obtain the methyl N-benzyl-N-tosyl-alaninate S13. Colorless oil (2.74 g, 88%). Rf (EtOAc/hexane 3:7) = 0.54. [α]²² = −42.5 (c 2.5 CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ 1.26-1.28 (m, 3H, CH₃), 2.42 (br s, 3H, CH₃), 3.42 (br s, 3H, CH₃), 4.42 (br d, 1H, J = 14.5 Hz, CHPh), 4.55 (br d, 1H, J = 16.0 Hz, CHPh), 4.61-4.63 (m, 1H, CH), 7.23-7.32 (m, 7H, 7CH₃Ar), 7.71 (br d, 2H, J = 5.5 Hz, 2CH₃Ar). ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 16.4, 21.5, 49.1, 52.0, 55.0, 127.4, 127.5, 128.0, 128.3, 129.5, 137.1, 137.3, 143.4, 171.6. IR (νmax/cm⁻¹) 2950 (w), 1742 (s), 1456 (m), 1339 (s), 1152 (s), 1089 (m), 845 (m), 725 (s), 655 (s). HRMS (ESI-TOF) m/z calcd for C₁₈H₂₁NO₄NaS [M + Na]⁺ 370.1089, found 370.1073.

**General Procedure A. Allenylation of Chiral N-Boc α-Amino Aldehydes and Subsequent Base-Catalyzed Cyclization.** To a solution of allenylboronic acid pinacol ester 1 (1.1 equiv.) and the amino aldehydes 2a-2f in toluene at 0 °C, was added Et₂Zn (1 M in toluene, 10 mol%) under nitrogen. The suspension was then stirred at 0 °C for 18 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution, and washed with saturated aqueous NaHCO₃ solution (15 mL) and water (10 mL). The organic layer was dried (Na₂SO₄), concentrated under reduced pressure and purified by flash column chromatography (EtOAc/hexane) to afford the allenyl amino alcohol products 9a-9f. To a solution of the allenyl product in dry THF was added sodium hydride (60% in mineral oil, 2.0 equiv.) at 0 °C and the reaction mixture was stirred at room temperature for 90 min. The reaction mixture was quenched by saturated aqueous NH₄Cl solution, washed with water (10 mL), dried
(MgSO₄), and then purified by flash column chromatography (acetone/n-pentane) to afford the corresponding oxazolidinone products 23a-23f.

**tert-Butyl ((2S,3S)-3-hydroxyhexa-4,5-dien-2-yl)carbamate (9a).** The title compound 9a was obtained after flash column chromatography (EtOAc/hexane 3:7) as a 2.6:1 mixture of syn and anti diastereomers following the general procedure A using tert-butyl (1-oxopropan-2-yl)carbamate 2a (0.06 g, 0.34 mmol), allenylboronic acid pinacol ester 1 (69.0 µL, 0.37 mmol, 1.1 equiv.) and Et₂Zn (1 M in toluene, 35.7 µL, 0.034 mmol, 10 mol%) in dry toluene (1 mL). Yellow oil (0.067 g, 92%). R_f (EtOAc/hexane 3:7) = 0.36. **¹H NMR** (500 MHz, CDCl₃) (mixture of two allene diastereomers, relative integrations given for each diastereomer) δ 1.12 (d, 3H, J = 6.5 Hz, CH₃, minor isomer), 1.19 (d, 3H, J = 7.0 Hz, CH₃, major isomer), 1.44 (s, 9H, C(CH₃)₃, for each isomer), 2.87 (br s, 1H, OH, major isomer), 3.17 (br s, 1H, OH, minor isomer), 3.71-3.75 (m, 1H, CH, major isomer), 3.75-3.82 (m, 1H, CH, minor isomer), 4.09 (br s, 1H, CH, major isomer), 4.23 (br s, 1H, CH, minor isomer), 4.86-4.90 (m, 2H, CH₂=C=, for each isomer), 5.16-5.28 (m, 1H, CH=C=, for each isomer). **¹³C{¹H} NMR** (125 MHz, CDCl₃) (mixture of two allene diastereomers, minor indicated by asterisk) δ 18.8, 19.9, 20.1, 28.3, 29.8, 30.0*, 60.4, 60.8*, 69.3, 69.4*, 76.8, 79.1, 79.2*, 90.7*, 93.0, 156.6, 156.7*, 207.4, 207.9*. **IR** (ν max/cm⁻¹) 3378 (w), 2976 (w), 1555 (w), 1683 (s), 1506 (m), 1365 (m), 1257 (m), 1162 (s), 1051 (s), 1024 (s). **HRMS** (ESI-TOF) m/z calcd for C₁₁H₁₈NO₃ [M − H]⁺ 212.1287, found 212.1289.

**(4S,5S)-4-Methyl-5-(propa-1,2-dien-1-yl)oxazolidin-2-one (23a).** The title compound 23a was obtained as a single diastereomer following the general procedure A using 9a (0.060 g, 0.28 mmol) and sodium hydride (60% in mineral oil, 18.81 mg,
0.56 mmol, 2.0 equiv.) in THF (1 mL). Colorless oil (0.024 g, 61%). *R* (2% CH₂Cl₂/Et₂O) = 0.52. [α]°D = −30.3 (c 1.2 CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ 1.28 (d, 3H, *J* = 6.0 Hz, CH₃), 3.75-3.80 (m, 1H, CH), 4.55 (t, 1H, *J* = 6.5, 7.0 Hz, CH), 4.93-5.00 (m, 2H, CH₂=C=), 5.32 (q, 1H, *J* = 7.0 Hz, CH=C=), 6.02 (br s, 1H, NH). ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 20.0, 54.0, 78.6, 81.6, 89.0, 158.9, 209.2. IR (νmax/cm⁻¹) 3272 (m), 2926 (w), 1955 (w), 1739 (s), 1378 (m), 1003 (s), 942 (s), 855 (s), 770 (m). HRMS (ESI-TOF) m/z calcd for C₇H₉NO₂Na [M + Na]⁺ 162.0531, found 162.0537.

**tert-Butyl ((4S,5S)-5-hydroxyocta-6,7-dien-4-yl)carbamate (9b).** The title compound 9b was obtained after flash column chromatography (EtOAc/hexane 2:8) as a 5.2:1 mixture of syn and anti diastereomers following the general procedure A using tert-butyl(1-oxopentan-2-yl)carbamate 2b (0.149 g, 0.74 mmol), allenylboronic acid pinacol ester 1 (155.6 µL, 0.81 mmol, 1.1 equiv.) and Et₂Zn (1 M in toluene, 79.17 µL, 0.074 mmol, 10 mol%) in dry toluene (2 mL). Colorless oil (0.145 g, 81%). *R* (EtOAc/hexane 2:8) = 0.45. ¹H NMR (500 MHz, CDCl₃) (mixture of two allene diastereomers, relative integrations given for each diastereomer) δ 0.92 (t, 3H, *J* = 7.0 Hz, CH₃, for each isomer), 1.31-1.40 (m, 3H, CH and CH₂, for each isomer), 1.43 (s, 9H, C(CH₃)₃, for each isomer), 1.50-1.56 (m, H, CH, for each isomer), 3.00 (br s, 1H, OH, minor isomer), 3.17 (br s, 1H, OH, major isomer), 3.59 (br s, 1H, CH, major isomer), 3.70-3.73 (m, 1H, CH, minor isomer), 4.16 (br s, 1H, CH, major isomer), 4.23 (br s, 1H, CH, minor isomer), 4.85-4.90 (m, 2H, CH₂=C=, major isomer), 4.94-4.96 (m, 2H, CH₂=C=, minor isomer), 5.18-5.27 (m, 1H, CH=C=, for each isomer). ¹³C{¹H} NMR (125 MHz, CDCl₃) (mixture of two allene diastereomers, minor indicated by asterisk) δ 13.9, 19.3, 28.3, 34.0, 34.2*, 54.9,
55.2°, 70.2°, 71.4, 77.3, 79.2, 79.4°, 90.5°, 92.3, 156.4, 156.5°, 207.6. IR (ν_{max}/cm^{-1})
3380 (m), 2959 (m), 1955 (m), 1683 (s), 1365 (s), 1248 (s), 1166 (s), 1055 (s), 1018 (s), 843 (s). HRMS (ESI-TOF) m/z calcd for C_{13}H_{23}NO_{3}Na [M + Na]^+ 264.1576, found 264.1573.

(4S,5S)-5-(Propa-1,2-dien-1-yl)-4-propyloxazolidin-2-one (23b). The title compound 23b was obtained as a single diastereomer after column chromatography (acetone/n-pentane 2:8) following the general procedure A using 9b (0.067 g, 0.28 mmol) and sodium hydride (60% in mineral oil, 18.81 mg, 0.56 mmol, 2.0 equiv.) in THF (1 mL). Colorless oil (0.026 g, 55%). R_{f} (acetone/n-pentane 2:8) = 0.45. [α]_{D}^{22} = −24.9 (c 1.3 CHCl_{3}). ^{1}H NMR (500 MHz, CDCl_{3}) δ 0.95 (t, 3H, J = 7.0, 7.5 Hz, C{H{3}}), 1.32-1.43 (m, 2H, CH_{2}), 1.54-1.57 (m, 2H, CH_{2}), 3.67 (q, 1H, J = 6.5 Hz, CH), 4.62-4.65 (m, 1H, CH), 4.96-4.99 (m, 2H, CH_{2}=C=), 5.34 (q, 1H, J = 6.5, 7.0 Hz, CH=C=), 6.51 (br s, 1H, NH). ^{13}C{[^{1}H]} NMR (125 MHz, CDCl_{3}) δ 73.7, 78.6, 96.7, 117.8, 138.4, 140.0, 149.4, 219.0, 268.8. IR (ν_{max}/cm^{-1}) 3266 (m), 2959 (m), 2932 (m), 1955 (m), 1742 (s), 1387 (s), 1239 (s), 1239 (s), 978 (s), 852 (s), 767 (s). HRMS (ESI-TOF) m/z calcd for C_{9}H_{12}NO_{2} [M − H]^+ 166.0862, found 166.0870.

**tert-Butyl ((4S,5S)-5-hydroxy-2-methylocta-6,7-dien-4-yl)carbamate (9c).**
The title compound 9c was obtained after flash column chromatography (EtOAc/hexane 2:8) as a 5.7:1 mixture of syn and anti diastereomers following the general procedure A using tert-butyl (4-methyl-1-oxopentan-2-yl)carbamate 2c (0.18 g, 0.83 mmol), allenylboronic acid pinacol ester 1 (176.56 µL, 0.92 mmol, 1.1 equiv.) and Et_{2}Zn (1 M in toluene, 88.80 µL, 0.083 mmol, 10 mol%) in dry toluene (2 mL). White solid (0.172 g, 81%). Mp = 38-40 °C. R_{f} (EtOAc/hexane 2:8) = 0.37. ^{1}H NMR
(500 MHz, CDCl$_3$) (mixture of two allene diastereomers, relative integrations given for each diastereomer) $\delta$ 0.92 (d, 6H, $J = 6.0$ Hz, 2CH$_3$, for each isomer), 1.27-1.39 (m, 1H, CH, for each isomer), 1.43 (s, 9H, C(CH$_3$)$_3$, for each isomer), 1.65-1.68 (m, 2H, CH$_2$, for each isomer), 3.11 (br s, 1H, OH, major isomer), 2.95 (br s, 1H, OH, minor isomer), 3.68 (br s, 1H, CH, major isomer), 3.70-3.80 (br s, 1H, CH, minor isomer), 4.12 (br s, 1H, CH, major isomer), 4.22 (br s, 1H, CH, minor isomer), 4.79-4.90 (m, 2H, CH$_2$=C=, for each isomer), 5.18-5.20 (m, 1H, CH=C=, minor isomer), 5.25-5.27 (m, 1H, CH=C=, major isomer). $^{13}$C{$_1^1$H} NMR (125 MHz, CDCl$_3$) (mixture of two allene diastereomers, minor indicated by asterisk) $\delta$ 22.0*, 23.2, 24.8, 28.3, 40.8, 41.3*, 53.2, 53.9*, 71.7, 72.5*, 76.8, 79.2, 79.7*, 91.2*, 92.3, 156.3, 156.5*, 207.6. IR ($\nu_{\text{max}}$/cm$^{-1}$) 3361 (m), 2956 (m), 1955 (m), 1682 (s), 1504 (s), 1365 (s), 1248 (s), 1166 (s), 1047 (s), 843 (s). HRMS (ESI-TOF) $m$/z calcd for C$_{14}$H$_{25}$NO$_3$Na [M + Na]$^+$ 278.1732, found 278.1720.

(4S,5S)-4-Isobutyl-5-(propa-1,2-dien-1-yl)oxazolidin-2-one (23c). The title compound 23c was obtained as a single diastereomer after column chromatography (acetone/n-pentane 2:8) following the general procedure A using 9c (0.05 g, 0.195 mmol) and sodium hydride (60% in mineral oil, 18.81 mg, 0.39 mmol, 2.0 equiv.) in THF (1 mL). Colorless oil (0.021 g, 58%). $R_f$ (acetone/n-pentane 2:8) = 0.30. [$\alpha$]$_D^{22}$ = −32.6 (c 1 CHCl$_3$). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 0.91-0.93 (m, 6H, 2CH$_3$), 1.38-1.43 (m, 1H, CH), 1.48-1.53 (m, 1H, CH), 1.61-1.68 (m, 1H, CH), 3.70-3.74 (m, 1H, CH), 4.58-4.61 (m, 1H, CH), 4.93-5.00 (m, 2H, CH$_2$=C=), 5.33 (q, 1H, $J = 6.5$ Hz, CH=C=), 6.28 (br s, 1H, NH). $^{13}$C{$_1^1$H} NMR (125 MHz, CDCl$_3$) $\delta$ 22.2, 23.1, 25.2, 44.1, 56.5, 78.6, 80.5, 89.5, 159.1, 209.1. IR ($\nu_{\text{max}}$/cm$^{-1}$) 3256 (m), 2962 (m), 1956 (w), 1742 (s), 1387 (m), 1228 (m), 993 (m), 852 (m), 734 (m). HRMS (ESI-TOF) $m$/z calcd for C$_{16}$H$_{25}$NO$_2$Na [M + Na]$^+$ 204.0995, found 204.0996.
**tert-Butyl ((3S,4S)-4-hydroxy-2-methylhepta-5,6-dien-3-yl)carbamate (9d).** The title compound 9d was obtained after flash column chromatography (EtOAc/hexane 2:8) as a 9:1 mixture of *syn* and *anti* diastereomers following the general procedure A using tert-butyl (3-methyl-1-oxobutan-2-yl)carbamate 2d (0.10 g, 0.496 mmol), allenylboronic acid pinacol ester 1 (103.75 µL, 0.54 mmol, 1.1 equiv.) and Et₂Zn (1 M in toluene, 37.14 µL, 0.035 mmol, 7 mol%) in dry toluene (1 mL). White solid (0.106 g, 88%). Mp = 39-41 °C. Rₐ (EtOAc/hexane 2:8) = 0.35. ¹H NMR (500 MHz, CDCl₃) (mixture of two allene diastereomers, relative integrations given for each diastereomer) δ 0.94 (d, 3H, J = 6.5 Hz, CH₃, for each isomer), 0.99 (d, 3H, J = 6.5 Hz, CH₃, for each isomer), 1.44 (s, 9H, C(CH₃)₃, for each isomer), 1.87-1.93 (m, 1H, CH, for each isomer), 2.68 (br s, 1H, OH, minor isomer), 2.80 (br s, 1H, OH, major isomer), 3.20-3.23 (m, 1H, CH, minor isomer), 3.26-3.29 (m, 1H, CH, major isomer), 4.28 (br s, 1H, CH, minor isomer), 4.33 (br s, 1H, CH, major isomer), 4.85-4.93 (m, 2H, CH=CH=, for each isomer), 5.19-5.21 (m, 1H, CH=CH=, major isomer), 5.25-5.26 (m, 1H, CH=CH=, major isomer). ¹³C{¹H} NMR (125 MHz, CDCl₃) (mixture of two allene diastereomers, minor indicated by asterisk) δ 18.8, 19.9, 20.1, 28.3, 29.8, 30.0*, 60.4, 60.8*, 69.3, 69.4*, 76.8, 79.1, 79.2*, 90.7*, 93.0, 156.6, 156.7*, 207.4, 207.9*. IR (νmax/cm⁻¹) 3373 (m), 2979 (m), 2361 (m), 1955 (w), 1662 (s), 1525 (s), 1367 (s), 1245 (s), 1166 (s), 1018 (m), 869 (m), 684 (m). HRMS (ESI-TOF) m/z calcd for C₁₃H₂₃NO₃Na [M + Na]⁺ 264.1576, found 264.1581.

**(4S,5S)-4-Isopropyl-5-(propa-1,2-dien-1-yl)oxazolidin-2-one (23d).** The title compound 23d was obtained as a 4.3:1 mixture of two diastereomers after column chromatography (acetone/n-pentane 2:8) following the general procedure A.
using 9d (0.10 g, 0.414 mmol) and sodium hydride (60% in mineral oil, 27.88 mg, 0.83 mmol, 2.0 equiv.) in THF (1 mL). Milky oil (0.106 g, 74%). Rf (acetone/n-pentane 2:8) = 0.44. 1H NMR (500 MHz, CDCl3) (mixture of two diastereomers, relative integrations given for each diastereomer) δ 0.94 (br d, 3H, J = 6.5 Hz, CH3, major isomer), 0.98 (br d, 3H, J = 6.0 Hz, CH3, major isomer), 0.99 (br d, 3H, J = 6.0 Hz, CH3, minor isomer), 1.77 (br s, 1H, CH, major isomer), 1.90 (br s, 1H, CH, minor isomer), 3.45 (br s, 1H, CH, major isomer), 3.61-3.63 (m, 1H, CH, major isomer), 4.74 (br s, 1H, CH, major isomer), 4.92-4.97 (m, 2H, CH2=C=, for each isomer), 5.04-5.06 (m, 1H, CH, minor isomer), 5.32-5.37 (m, 1H, CH=C=, for each isomer), 6.58 (br s, 1H, NH, minor isomer), 6.66 (br s, 1H, NH, major isomer). 13C{1H} NMR (125 MHz, CDCl3) (mixture of two diastereomers, minor indicated by asterisk) δ 17.93, 17.97, 28.1*, 32.3, 62.3*, 63.5, 75.5*, 78.0, 78.6, 78.7*, 85.9*, 90.4, 159.1, 159.8*, 208.7, 210.0*. IR (νmax/cm⁻¹) 3260 (m), 2963 (m), 1955 (w), 1743 (s), 1387 (m), 1228 (m), 993 (m), 851 (m), 734 (m). HRMS (ESI-TOF) m/z calcd for C9H13NO2Na [M + Na]+ 190.0838, found 190.0840.

tert-Butyl ((2S,3S)-3-hydroxy-1-phenylhexa-4,5-dien-2-yl)carbamate (9e).
The title compound 9e was obtained after flash column chromatography (EtOAc/hexane 3:7) as a 2.5:1 mixture of syn and anti diastereomers following the general procedure A using tert-butyl (1-oxo-3-phenylpropan-2-yl)carbamate 2e (0.093 g, 0.373 mmol), allenylboronic acid pinacol ester 1 (78.78 µL, 0.41 mmol, 1.1 equiv.) and Et2Zn (1 M in toluene, 40.00 µL, 0.0373 mmol, 10 mol%) in dry toluene (1 mL). White solid (0.087 g, 80%). Mp = 60-62 °C. Rf (EtOAc/hexane 3:7) = 0.53. 1H NMR (500 MHz, CDCl3) (mixture of two allene diastereomers, relative integrations given for each diastereomer) δ 1.36 (s, 9H, C(CH3)3, minor isomer), 1.43
(s, 9H, C(CH$_3$)$_3$, major isomer), 2.61 (br s, 1H, OH, major isomer), 2.88-2.96 (m, 2H, CH$_2$Ph, for each isomer), 3.76 (br s, 1H, CH, minor isomer), 3.82 (br s, 1H, CH, major isomer), 4.15 (br s, 1H, CH, major isomer), 4.27 (br s, 1H, CH, minor isomer), 4.85-4.91 (m, 2H, CH$_2$=C=, for each isomer), 5.24-5.29 (m, 1H, CH=C=, for each isomer), 7.19-7.29 (m, 5H, 5CH$_2$Ar, for each isomer). $^{13}$C($^1$H) NMR (125 MHz, CDCl$_3$) (mixture of two allene diastereomers, minor indicated by asterisk) $\delta$ 28.5, 36.1*, 38.2, 56.1*, 56.4, 69.4, 77.9*, 78.0, 79.4, 79.8*, 91.2*, 92.6, 126.3*, 126.6, 128.4, 129.2*, 129.32*, 129.37, 138.0*, 138.2, 156.0, 207.4*, 207.6. IR (v$_{max}$/cm$^{-1}$) 3379 (m), 2981 (w), 2358 (s), 1954 (w), 1675 (s), 1521 (s), 1452 (m), 1248 (s), 1168 (s), 1002 (m), 837 (s), 759 (m), 703 (s). HRMS (ESI-TOF) m/z calcd for C$_{17}$H$_{24}$NO$_3$ [M + H]$^+$ 290.1756, found 290.1751.

(4S,5S)-4-Benzyl-5-(propa-1,2-dien-1-yl)oxazolidin-2-one (23e). The title compound 23e was obtained as a 3:1 mixture of two diastereomers after column chromatography (acetone/n-pentane 2:8) following the general procedure A using 9e (0.087 g, 0.30 mmol) and sodium hydride (60% in mineral oil, 20.16 mg, 0.60 mmol, 2.0 equiv.) in THF (1 mL). Colorless oil (0.041 g, 63%). R$_f$ (acetone/n-pentane 2:8) = 0.31. $^1$H NMR (500 MHz, CDCl$_3$) (mixture of two diastereomers, relative integrations given for each diastereomer) $\delta$ 2.70-2.75 (m, 2H, CH$_2$Ph, minor isomer), 2.86-2.90 (m, 2H, CH$_2$Ph, major isomer), 3.90 (q, 1H, $J$ = 6.5 Hz, CH, major isomer), 4.10-4.14 (m, 1H, CH, minor isomer), 4.72 (t, 1H, $J$ = 6.0 Hz, CH, major isomer), 4.84-4.93 (m, 2H, CH$_2$=C=, major isomer), 4.96-4.98 (m, 2H, CH$_2$=C=, minor isomer), 5.13 (t, 1H, $J$ = 8.0 Hz, CH, minor isomer), 5.24 (q, 1H, $J$ = 6.5, 7.0 Hz, CH=C=, major isomer), 5.35 (q, 1H, $J$ = 7.0 Hz, CH=C=, minor isomer), 5.65 (br s, 1H, NH, minor isomer), 6.19 (br s, 1H, NH, major isomer), 7.16 (d, 2H, $J$ = 7.5 Hz,
$2CH_{Ar}$, for each isomer), 7.22-7.25 (m, 1H, $CH_{Ar}$, for each isomer), 7.29-7.32 (m, 2H, $2CH_{Ar}$, for each isomer). $^{13}$C{$^1$H} NMR (125 MHz, CDCl$_3$) (mixture of two diastereomers, minor indicated by asterisk) $\delta$ 37.5*, 40.9, 57.5*, 59.3, 78.0*, 78.3*, 78.7, 79.3, 86.3*, 89.5, 127.33, 127.39*, 129.10, 129.18*, 129.2*, 129.4, 136.0, 136.9*, 158.7, 209.0, 210.0*. IR ($\nu_{max}$/cm$^{-1}$) 3267 (w), 2917 (w), 1955 (w), 1386 (m), 1230 (m), 992 (s), 854 (s), 699 (s). HRMS (ESI-TOF) m/z calcd for C$_{13}$H$_{13}$NO$_2$Na [M + Na]$^+$ 238.0838, found 238.0840.

tert-Butyl 3-((2S,3S)-2-((tert-butoxycarbonyl)amino)-3-hydroxyhexa-4,5-dien-1-y1)-1H-indole-1-carboxylate (9f). The title compound 9f was obtained after flash column chromatography (EtOAc/hexane 2:8) as a 2.5:1 mixture of syn and anti diastereomers following the general procedure A using tert-butyl 3-(2-((tert-butoxycarbonyl)amino)-3-oxopropyl)-1H-indole-1-carboxylate 2f (0.05 g, 0.128 mmol), allenylboronic acid pinacol ester 1 (27.00 µL, 0.14 mmol, 1.1 equiv.) and Et$_2$Zn (1 M in toluene, 14.00 µL, 0.0128 mmol, 10 mol%) in dry toluene (1 mL). Colorless oil (0.043 g, 78%). $R_f$ (EtOAc/hexane 2:8) = 0.33. $^1$H NMR (500 MHz, CDCl$_3$) (mixture of two allene diastereomers, relative integrations given for each diastereomer) $\delta$ 1.39 (s, 9H, C(CH$_3$)$_3$, minor isomer), 1.42 (s, 9H, C(CH$_3$)$_3$, major isomer), 1.65 (s, 9H, C(CH$_3$)$_3$, for each isomer), 2.52 (br s, 1H, O$H$, major isomer), 2.91-3.06 (m, 2H, $CH_2$, for each isomer), 3.93 (br s, 1H, $CH$, major isomer), 4.06 (br s, 1H, $CH$, minor isomer), 4.23 (br s, 1H, $CH$, major isomer), 4.32 (br s, 1H, $CH$, minor isomer), 4.87-5.04 (m, 2H, $CH_2$=C=, for each isomer), 5.26-5.32 (m, 1H, $CH$=C=, for each isomer), 7.22-7.66 (m, 4H, 4$CH_{Ar}$, for each isomer), 8.13 (br s, 1H, $CH_{Ar}$, for each isomer). $^{13}$C{$^1$H} NMR (125 MHz, CDCl$_3$) (mixture of two allene diastereomers, minor indicated by asterisk) $\delta$ 28.2, 28.3*, 54.7, 55.3*, 69.3, 71.7*, 28.3, 28.3*,
78.1*, 78.3, 79.5, 79.8*, 83.5, 91.3*, 92.6, 115.21, 115.27*, 116.8*, 117.0, 119.0, 119.2*, 122.5, 123.9, 124.41, 124.46*, 130.7, 135.4, 149.7, 156.1, 207.4, 207.5*. IR (ν\textsubscript{max}/cm\textsuperscript{-1}) 3385 (w), 2975 (w), 2930 (w), 1955 (w), 1730 (s), 1684 (s), 1507 (m), 1452 (s), 1367 (s), 1252 (s), 1157 (s), 1085 (s), 1015 (m), 852 (m), 744 (s).

HRMS (ESI-TOF) m/z calcd for C\textsubscript{24}H\textsubscript{32}N\textsubscript{2}O\textsubscript{5}Na [M + Na]\textsuperscript{+} 451.2209, found 451.2227.

\textit{tert}-Butyl 3-(((4R,5R)-2-oxo-5-(propa-1,2-dien-1-yl)oxazolidin-4-yl)methyl)-1H-indole-1-carboxylate (23f). The title compound 23f was obtained as a single diastereomer after careful column chromatography (acetone/n-pentane 2:8) following the general procedure A using 9f (0.036 g, 0.084 mmol) and sodium hydride (60% in mineral oil, 5.68 mg, 0.168 mmol, 2.0 equiv.) in THF (1 mL). Colorless gummy oil (0.015 g, 50%). R\textsubscript{f} (acetone/n-pentane 2:8) = 0.26. [α]\textsubscript{D}\textsuperscript{2} = –35.8 (c 0.7 CHCl\textsubscript{3}). \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) δ 1.68 (s, 9H, C(CH\textsubscript{3})\textsubscript{3}), 2.90-2.94 (m, 1H, CH), 3.00-3.04 (m, 1H, CH), 4.03 (br s, 1H, CH), 4.81 (br s, 1H, CH), 4.96 (br s, 2H, CH\textsubscript{2}=C=), 5.19 (br s, 1H, NH), 5.37 (br d, 1H, J = 6.5 Hz, CH=C=), 7.26 (br s, 1H, CH\textsubscript{Ar}), 7.34-7.37 (m, 1H, CH\textsubscript{Ar}), 7.46 (br s, 2H, 2CH\textsubscript{Ar}), 8.15 (br s, 1H, CH\textsubscript{Ar}). \textsuperscript{13}C{\textsuperscript{1}H} NMR (125 MHz, CDCl\textsubscript{3}) δ 28.2, 30.5, 57.5, 78.8, 79.4, 84.0, 89.2, 114.9, 115.5, 118.5, 122.8, 123.9, 124.9, 129.7, 135.6, 149.4, 157.7, 208.8. IR (ν\textsubscript{max}/cm\textsuperscript{-1}) 3277 (w), 2982 (w), 2357 (w), 1955 (w), 1751 (s), 1730 (s), 1570 (s), 1428 (s), 1368 (s), 1255 (s), 1155 (s), 1086 (m), 854 (m). HRMS (ESI-TOF) m/z calcd for C\textsubscript{20}H\textsubscript{23}N\textsubscript{2}O\textsubscript{4} [M + H]\textsuperscript{+} 355.1658, found 355.1664.

2S,3S)-2-(Tritylamino)hexa-4,5-dien-3-ol (12). The title compound 12 was obtained after flash column chromatography (Et\textsubscript{2}O/hexane 2:8) as a 1:3:1 mixture of \textit{syn} and \textit{anti} diastereomers following the general procedure A using 2-
(tritylamino)propanal 5 (0.10 g, 0.317 mmol), allenylboronic acid pinacol ester 1 (78.00 µL, 0.41 mmol, 1.1 equiv.) and Et₂Zn (1 M in toluene, 34.0 µL, 0.0317 mmol, 10 mol%) in dry toluene (1 mL). Colorless oil (0.093 g, 82%). Rᵣ (Et₂O/hexane 2:8) = 0.41. ¹H NMR (300 MHz, CDCl₃) (mixture of two allene diastereomers, relative integrations given for each diastereomer) δ 0.43 (d, 3H, J = 6.0 Hz, CH₃, minor isomer), 0.75 (d, 3H, J = 6.6 Hz, CH₃, major isomer), 2.23 (br s, 1H, NH, for each isomer), 2.69-2.77 (m, 1H, CH, for each isomer), 3.40-3.43 (m, 1H, CH, for each isomer), 4.74-4.77 (m, 2H, CH₂=C, major isomer), 4.80-4.83 (m, 2H, CH₂=C, minor isomer), 4.98 (q, 1H, J = 6.0, 6.3 Hz, CH=C, major isomer), 5.22 (q, 1H, J = 6.6, 6.6 Hz, CH=C, minor isomer), 7.15-7.28 (m, 10H, 10CH₃Ar, for each isomer), 7.54 (d, 5H, J = 7.8 Hz, 5CH₃Ar, for each isomer). ¹³C{¹H} NMR (75 MHz, CDCl₃) (mixture of two allene diastereomers, minor indicated by asterisk) δ 15.9, 17.1*, 52.6, 53.0*, 71.2, 71.3*, 73.2*, 76.6, 91.7*, 92.2, 126.4, 127.9, 128.7, 128.8*, 146.73, 146.76*, 207.1, 207.9*. IR (νmax/cm⁻¹) 3385 (w), 3056 (w), 2970 (w), 1952 (m), 1490 (s), 1447 (s), 1031 (s), 845 (s), 744 (s), 705 (s). HRMS (ESI-TOF) m/z calcd for C₂₅H₂₆NO [M + H]+ 356.2014, found 356.2011.

**General Procedure B. Allenylation of Chiral N,N-[((tert-butoxy)carbonyl)benzyl] amino aldehydes and Subsequent Gold-Catalyzed Cyclization.** To a solution of allenylboronic acid pinacol ester 1 (1.3 equiv.) and the amino aldehydes 6a-g in toluene at 0 °C, was added Et₂Zn (1 M in toluene, 10 mol%) under nitrogen. The suspension was then stirred at 0 °C for 18 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (5 mL), and then washed with saturated aqueous NaHCO₃ solution (15 mL) and water (10 mL). The organic layer was dried (Na₂SO₄), and then concentrated under reduced pressure to afford the resulting allenyl amino
alcohol product 13. Then, to a solution of this crude product in dry dichloroethane was added AuPPh₃NTf₂ (10 mol%). The reaction was stirred at 60 °C for 8 h and then filtered through a pad of silica gel and after removal of the solvent the crude product was used in the next step without purification. Chlorotrimethylsilane (5 equiv.) was added to a solution of the crude dihydrofuran in dry methanol. The reaction mixture was stirred at room temperature overnight, and then was neutralized by the addition of saturated aqueous NaHCO₃ solution to about pH = 7, followed by purification by flash column chromatography to afford the corresponding Boc-deprotected dihydrofuran products 25a-25g.

**tert-Butyl benzyl((2S,3R)-3-hydroxyhexa-4,5-dien-2-yl)carbamate (13).**

The title compound 13 was prepared following the first part of general procedure B (in this case was purified by column chromatography as part of the optimization study) using tert-butyl benzyl(1-oxopropan-2-yl)carbamate 6a (0.065 g, 0.24 mmol), allenylboronic acid pinacol ester 1 (61 µL, 0.32 mmol, 1.3 equiv.) and Et₂Zn (1 M in toluene, 25 µL, 0.024 mmol, 10 mol%) in dry toluene (2 mL). The crude product was purified by flash column chromatography (EtOAc/hexane 2:8) as a 19:1 mixture of anti and syn diastereomers. Colorless oil (0.07 g, 96%). \( R_f \) (EtOAc/hexane 2:8) = 0.31. \([\alpha]_D^{23} = +7.31 \) (c 7.2 CHCl₃). \(^1\text{H NMR} \) (500 MHz, CDCl₃) (mixture of rotamers) δ 1.17 (d, 0.7H, \( J = 7.0 \text{ Hz} \)), 1.20 (d, 2.3H, \( J = 7.0 \text{ Hz} \)), 1.33-1.45 (br s, 9H, C(CH₃)₃), 3.70-3.76 (m, 1H, CH), 4.01-4.12 (m, 0.7H), 4.35-4.49 (m, 3.3H), 4.80 (m, 2H, CH₂=CH=), 5.12-5.17 (m, 1H, CH=CH=2), 7.23-7.33 (m, 5H, 5CH₃). \(^{13}\text{C}^1\text{H} \) NMR (125 MHz, CDCl₃) (mixture of rotamers, minor rotamer indicated by asterisk) δ 11.9, 28.3, 51.1, 58.5*, 58.7, 72.9, 77.4, 80.6, 80.6*, 92.8, 127.0, 127.1, 127.3*, 128.4, 128.5*, 139.1, 156.7, 207.1. \(^\text{IR} \) (\( \nu_{\text{max}}/\text{cm}^{-1} \)) 3473 (m), 2976 (m), 1956 (m), 1680 (s),
(2S,3R)-2-(Dibenzylamino)hexa-4,5-dien-3-ol (15). The major diastereomer of the title compound 15 was obtained after purification by flash column chromatography (Et2O/hexane 1:9) following the general procedure B using 2-(dibenzylamino)propanal 8 (0.096 g, 0.339 mmol), allenylboronic acid pinacol ester 1
(84.00 µL, 0.44 mmol, 1.3 equiv.) and Et₂Zn (1 M in toluene, 36.00 µL, 0.0339 mmol, 10 mol%) in dry toluene (1 mL). Colorless oil (0.05 g, 50%). \( R_f \) (Et₂O/hexane 1:9) = 0.25. \( [\alpha]_D^{22} = -36.2 \) (c 4.1 CHCl₃). \(^1\)H NMR (500 MHz, CDCl₃) \( \delta \) 1.12 (d, 3H, \( J = 11.5 \) Hz, \( CH_3 \)), 2.85-2.89 (m, 1H, \( CH \)), 3.42 (d, 2H, \( J = 23.0 \) Hz, \( 2CHPh \)), 3.82 (d, 2H, \( J = 23.0 \) Hz, \( 2CHPh \)), 4.07-4.12 (m, 1H, \( CH \)), 4.77-4.81 (m, 2H, \( CH_2=C= \)), 5.30 (q, 1H, \( J = 10.5, 10.5 \) Hz, \( CH=C= \)), 7.19-7.34 (m, 10H, 10\( CH_Ar \)). \(^{13}\)C\(^{1}\)H NMR (125 MHz, CDCl₃) \( \delta \) 9.2, 54.9, 57.7, 71.1, 76.8, 93.6, 127.2, 128.5, 129.0, 139.9, 207.6. IR (\( \nu_{\max}/cm^{-1} \)) 3379 (w), 3027 (w), 2926 (w), 2801 (w), 1952 (m), 1452 (m), 1368 (m), 1244 (w), 1027 (s), 845 (s), 744 (s), 696 (s). HRMS (ESI-TOF) \( m/z \) calcd for \( C_{20}H_{24}NO \) [M + H]⁺ 294.1858, found 294.1852.

\( (4S,5R)\)-3-Benzyl-4-methyl-5-(propa-1,2-dien-1-yl)oxazolidin-2-one  \( (24) \). To a solution of the allenyl product 13 (0.09 g, 0.29 mmol) in dry THF (1 mL) was added sodium hydride (60% in mineral oil, 16.00 mg, 0.59 mmol, 2.0 equiv.) at 0 °C. The reaction was stirred at room temperature for 60 min. Then, the reaction mixture was quenched with saturated aqueous NH₄Cl solution (5 mL), washed with water (10 mL) and dried (MgSO₄). Purification by flash column chromatography (EtOAc/hexane 3:7) afforded the corresponding oxazolidinone product 24. Light yellow oil (0.035 g, 52%). \( R_f \) (EtOAc/hexane 3:7) = 0.40. \( [\alpha]_D^{22} = -56.7 \) (c 1.7 CHCl₃). \(^1\)H NMR (300 MHz, CDCl₃) \( \delta \) 1.14 (d, 3H, \( J = 6.6 \) Hz, \( CH_3 \)), 3.69-3.78 (m, 1\( H, CH \)), 4.03 (d, 1\( H, J = 15.3 \) Hz, \( CHPh \)), 4.82 (d, 1\( H, J = 15.0 \) Hz, \( CHPh \)), 4.86-4.98 (m, 3\( H, CH=C= \) and \( CH \)), 5.17-5.24 (m, 1\( H, CH=C= \)), 7.25-7.37 (m, 5\( H, 5CH_Ar \)). \(^{13}\)C\(^{1}\)H NMR (75 MHz, CDCl₃) \( \delta \) 13.7, 45.7, 53.3, 76.1, 77.6, 86.1, 127.9, 128.0, 128.8, 135.9, 157.5, 209.7. IR (\( \nu_{\max}/cm^{-1} \)) 2924 (w), 2358 (w), 1358 (w), 1743 (s),
(S)-N-benzyl-1-((R)-2,5-dihydrofuran-2-yl)ethan-1-amine (25a). Following the general procedure B using 0.065 g, 0.24 mmol of 6a, the resulting crude of 13 was treated with AuPPh₃NTf₂ (17.50 mg, 0.024 mmol, 10 mol%), followed by Boc-deprotection of the crude product by treatment with chlorotrimethylsilane (0.14 mL, 1.20 mmol, 5 equiv.) in methanol (2 mL). The title compound 25a was obtained as a single diastereomer after purification by flash column chromatography (Et₂O/hexane 7:3). The isolated yield was calculated for the three steps starting from the aldehyde 6a. Colorless oil (0.03 g, 60%). \( R_f \) (Et₂O/hexane 7:3) = 0.15. The ee was determined by chiral HPLC of the corresponding alcohol using a Phenomenex Lux Cellulose-3 column; hexane/isopropanol (98:2); flow rate = 0.5 mL/min; 210 nm; \( t_{\text{major}} \) = 9.83 min, \( t_{\text{minor}} \) = 10.95 min, 91% ee. \( [\alpha]_D^{25} = +104.5 \) (c 0.9 CHCl₃). \(^1\)H NMR (500 MHz, CDCl₃) \( \delta \) 1.06 (d, 3H, \( J = 6.5 \) Hz, \( CH_3 \)), 1.69 (s, 1H, \( NH \)), 2.85-2.88 (m, 1H, \( CH \)), 3.79 (d, 1H, \( J = 13.5 \) Hz, \( CHPh \)), 3.90 (d, 1H, \( J = 13.5 \) Hz, \( CHPh \)), 4.62-4.69 (m, 2H, \( CH_2 \)), 4.87-4.88 (m, 1H, \( CH \)), 5.81-5.82 (m, 1H, \( CH \)), 5.95-5.97 (m, 1H, \( CH \)), 7.21-7.33 (m, 5H, 5\( CH_\text{Ar} \)). \(^{13}\)C\(^{1}\)H NMR (125 MHz, CDCl₃) \( \delta \) 15.6, 51.4, 55.5, 75.7, 89.4, 126.8, 127.0, 127.7, 128.0, 128.3, 140.7. IR (\( \nu_{\text{max}}/\text{cm}^{-1} \)) 3327 (w), 3026 (w), 2964 (w), 2845 (m), 1683 (m), 1630 (m), 1494 (m), 1452 (m), 1355 (m), 1269 (m), 1068 (s), 1028 (s), 950 (s), 847 (m), 731 (s), 696 (s). HRMS (ESI-TOF) \( m/z \) calcd for C\(_{14}\)H\(_{15}\)NO \([M + \text{H}]^+\) 252.1000, found 252.1003.

(S)-N-benzyl-1-((R)-2,5-dihydrofuran-2-yl)butan-1-amine (25b). The allenyl precursor was prepared following B the general procedure using tert-butyl
benzyl(1-oxopentan-2-yl)carbamate 6b (0.485 g, 1.66 mmol), allenylboronic acid pinacol ester 1 (0.41 mL, 2.16 mmol, 1.3 equiv.) and Et₂Zn (1M in toluene, 180 µL, 0.048 mmol, 10 mol%) in dry toluene (5 mL). Following the general procedure B the crude allenyl product was treated with AuPPh₃NTf₂ (0.117 g, 0.16 mmol, 10 mol%) in dry dichloroethane (5 mL). Boc-deprotection of the resulting dihydrofuran with chlorotrimethylsilane (0.95 mL, 8.00 mmol, 5 equiv.) in methanol (5 mL) gave the title compound 25b as a 4.3:1 mixture of syn and anti diastereomers after purification by flash column chromatography (Et₂O/hexane 2:8). The isolated yield was calculated for the three steps starting from the aldehyde 6b. Colorless oil (0.26 g, 68%), Rₚ (Et₂O/hexane 2:8) = 0.30. ¹H NMR (300 MHz, CDCl₃) (mixture of two diastereomers, relative integrations given for each diastereomer) δ 0.88 (t, 3H, J = 6.30, 6.9 Hz, CH₃, for each isomer), 1.28-1.49 (br m, 2H, CH₂, for each isomer), 2.50-2.60 (m, 1H, CH, minor isomer), 2.69 (q, 1H, J = 8.5, 10.5 Hz, CH, major isomer), 3.80 (s, 2H, CH₂Ph, minor isomer), 3.83 (s, 2H, CH₂Ph, major isomer), 4.58-4.70 (m, 2H, CH₂, for each isomer), 4.84-4.86 (m, 1H, CH, minor isomer), 4.93-4.94 (m, 1H, CH, major isomer), 5.81-5.83 (m, 1H, CH=, for each isomer), 7.18-7.30 (m, 5H, 5CH₃Ar, for each isomer). ¹³C{¹H} NMR (75 MHz, CDCl₃) (mixture of two diastereomers, minor indicated by asterisk) δ 14.3, 14.4*, 19.3*, 19.5, 33.1*, 33.3, 51.8*, 52.3, 60.2, 60.3*, 75.3*, 75.4, 88.3*, 88.6, 126.7, 127.2, 127.4*, 127.7, 127.8, 128.0*, 128.2, 140.9. IR (νmax/cm⁻¹) 3735 (w), 2956 (m), 2871 (m), 1457 (m), 1354 (w), 1073 (s), 734 (s), 696 (s). HRMS (ESI-TOF) m/z calcd for C₁₅H₂₁NONa [M + Na]^⁺ 254.1521, found 254.1531.

(S)-N-benzyl-1-(((R)-2,5-dihydrofuran-2-yl)-3-methylbutan-1-amine (25c).

The allenyl precursor was prepared following B the general procedure using tert-butyl
benzyl(4-methyl-1-oxopentan-2-yl)carbamate 6c (0.198 g, 0.65 mmol), allenylboronic acid pinacol ester 1 (160 µL, 0.84 mmol, 1.3 equiv.) and Et₂Zn (1 M in toluene, 70 µL, 0.065 mmol, 10 mol%) in dry toluene (2 mL). Following the general procedure B the crude allenyl product was treated with AuPPh₃NTf₂ (44.90 mg, 0.06 mmol, 10 mol%) in dry dichloroethane (2 mL). Boc-deprotection of the resulting dihydrofuran with chlorotrimethylsilane (0.38 mL, 3.25 mmol, 5 equiv.) in methanol (3 mL) gave the title compound 25c as a 3.2:1 mixture of syn and anti diastereomers after purification by flash column chromatography (Et₂O/hexane 2:8). The isolated yield was calculated for the three steps starting from the aldehyde 6c. Colorless oil (0.097 g, 62%), Rᵣ (Et₂O/hexane 2:8) = 0.36. ¹H NMR (300 MHz, CDCl₃) (mixture of two diastereomers, relative integrations given for each diastereomer) δ 0.81-0.92 (m, 6H, 2CH₃, for each isomer), 1.22-1.33 (m, 1H, CH, for each isomer), 1.74-2.00 (m, 1H, CH, for each isomer), 2.77-2.81 (m, 1H, CH, major isomer), 2.85-2.89 (m, 1H, CH, minor isomer), 3.28 (s, 1H, NH, minor isomer), 3.34 (s, 1H, NH, major isomer), 3.82-3.92 (m, 2H, CH₂Ph, for each isomer), 4.65-4.69 (m, 2H, CH₂O, for each isomer), 4.97-5.00 (m, 1H, CH, for each isomer), 5.80-5.82 (m, 1H, CH=, for each isomer), 5.97-6.00 (m, 1H, CH=, for each isomer), 7.23-7.35 (m, 5H, 5CH₂Ar, for each isomer).

¹³C{¹H} NMR (75 MHz, CDCl₃) (mixture of two diastereomers, minor indicated by asterisk) δ 22.3, 23.5, 24.9, 40.4, 52.3, 54.0*, 58.2, 75.5, 88.8, 127.1, 126.8, 127.9*, 128.2, 128.33*, 128.36, 140.9. IR (νmax/cm⁻¹) 3735 (w), 2956 (m), 2926 (m), 2868 (m), 1457 (m), 1131 (m), 1074 (m), 740 (m), 697 (m), 619 (m). HRMS (ESI-TOF) m/z calcld for C₁₆H₂₄NO [M + H]+ 246.1858, found 246.1854.

(S)-N-benzyl-1-((R)-2,5-dihydrofuran-2-yl)-2-methylpropan-1-amine (25d). The allenyl precursor was prepared following the general procedure B using
**tert**-butyl benzyl(3-methyl-1-oxobutan-2-yl)carbamate 6d (0.53 g, 1.84 mmol), allenylboronic acid pinacol ester 1 (454 µL, 2.40 mmol, 1.3 equiv.) and Et₂Zn (1 M in toluene, 197 µL, 0.184 mmol, 10 mol%) in dry toluene (5 mL). Following the general procedure B the crude allenyl product was treated with AuPPh₃NTf₂ (0.13 g, 0.18 mmol, 10 mol%) in dry dichloroethane (5 mL). Boc-deprotection of the resulting dihydrofuran with chlorotrimethylsilane (1.12 mL, 9.20 mmol, 5 equiv.) in methanol (5 mL) gave the title compound 25d as a single diastereomer after purification by flash column chromatography (Et₂O/hexane 2:8). The isolated yield was calculated for the three steps starting from the aldehyde 6d. Colorless oil (0.263 g, 61%). R₆ (Et₂O/hexane 2:8) = 0.22. [α]D₂²² = -43.3 (c 0.65 CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ 0.98 (d, 6H, J = 6.5 Hz, 2CH₃), 1.84-1.87 (br m, 2H, CH, NH), 2.37 (br d, 1H, J = 3.0 Hz, CH), 3.83 (dd, 2H, J = 13.0, 12.5 Hz, CH₂Ph), 4.64 (br d, 2H, J = 13.0 Hz, CH₂), 4.95 (br s, 1H, CH), 5.80 (br s, 1H, CH=), 5.93 (br s, 1H, CH=), 7.22-7.32 (m, 5H, 5CHₐr). ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 19.28, 20.2, 30.7, 53.9, 65.7, 75.6, 87.9, 126.9, 127.2, 128.4, 129.2, 141.5. IR (νmax/cm⁻¹) 2955 (m), 2872 (m), 2359 (w), 1457 (m), 1070 (s), 1028 (s), 739 (s), 697 (s). HRMS (ESI-TOF) m/z calcd for C₁₅H₂₂NO [M + H]⁺ 232.1701, found 232.1703.

**(S)-N-benzyl-1-((R)-2,5-dihydrofuran-2-yl)-2-phenylethan-1-amine** (25e).

The allenyl precursor was prepared following the general procedure B using tert-butyl benzyl(1-oxo-3-phenylpropan-2-yl)carbamate 6e (0.278 g, 0.82 mmol), allenylboronic acid pinacol ester 1 (0.20 mL, 1.06 mmol, 1.3 equiv.) and Et₂Zn (1 M in toluene, 85.00 µL, 0.082 mmol, 10 mol%) in dry toluene (2 mL). Following the general procedure B the crude allenyl product was treated with AuPPh₃NTf₂ (60.00 mg, 0.08 mmol, 10 mol%) in dry dichloroethane (3 mL). Boc-deprotection of the
resulting dihydrofuran with chlorotrimethylsilane (0.52 mL, 4.10 mmol, 5 equiv.) in methanol (3 mL) gave the title compound **25e** as a 8.3:1 mixture of syn and anti diastereomers after purification by flash column chromatography (EtOAc/hexane 3:7). The isolated yield was calculated for the three steps starting from the aldehyde **6e**. Light yellow oil (0.133 g, 58%). **R**<sub>f</sub> (EtOAc/hexane 3:7) = 0.34. **1H NMR** (500 MHz, CDCl<sub>3</sub>) (mixture of two diastereomers, relative integrations given for each diastereomer) δ 2.70-2.74 (m, 1H, CHPh, for each isomer), 2.80-2.83 (m, 1H, CHPh, for each isomer), 2.90 (s, 1H, CH, minor isomer), 2.98 (br s, 1H, CH, major isomer), 3.77 (q, 2H, J = 13.5 Hz, CH<sub>2</sub>Ph, for each isomer), 4.63-4.73 (m, 2H, 2CH−O, for each isomer), 4.89 (br s, 1H, CH, for each isomer), 5.78 (br s, 1H, CH=, minor isomer), 5.89 (br s, 1H, CH=, major isomer), 5.98 (br s, 1H, CH=, for each isomer), 7.12-7.27 (m, 10H, 10CH<sub>Ar</sub>, for each isomer). **13C{1H} NMR** (125 MHz, CDCl<sub>3</sub>) (mixture of two diastereomers, minor indicated by an asterisk) δ 37.1, 37.4*, 52.10, 52.16*, 61.80, 61.85*, 75.5*, 75.6, 87.8*, 88.0, 126.1*, 126.2, 126.7, 127.2, 127.73*, 127.79*, 128.0, 128.3, 128.4, 129.3, 139.2, 139.5*, 140.5. **IR** (v<sub>max</sub>/cm<sup>−1</sup>) 3333 (w), 3026 (w), 2844 (m), 1494 (m), 1452 (m), 1070 (s), 739 (s), 696 (s). **HRMS** (ESI-TOF) m/z calcld for C<sub>19</sub>H<sub>22</sub>NO [M + H]<sup>+</sup> 280.1695, found 280.1697.

**tert-Butyl** 3-((S)-2-(benzylamino)-2-((R)-2,5-dihydrofuran-2-yl)ethyl)-1H-indole-1-carboxylate (**25f**). The allenyl precursor was prepared following the general procedure **B** using **tert-butyl** 3-(2-(benzyl(tert-butoxycarbonyl)amino)-3-oxopropyl)-1H-indole-1-carboxylate **6f** (0.389 g, 0.81 mmol), allenylboronic acid pinacol ester **1** (0.20 mL, 1.05 mmol, 1.3 equiv.) and Et<sub>2</sub>Zn (1 M in toluene, 87.30 µL, 0.081 mmol, 10 mol%) in dry toluene (3 mL). Following the general procedure **B** the crude allenyl product was treated with AuPPh<sub>3</sub>NTf<sub>2</sub> (59.15 mg, 0.08 mmol, 10 mol%) in dry
dichloroethane (4 mL). Boc-deprotection of the resulting dihydrofuran with chlorotrimethylsilane (0.52 mL, 4.05 mmol, 5 equiv.) in methanol (5 mL) gave the title compound 25f as a single diastereomer after purification by flash column chromatography (EtOAc/hexane 3:7). The isolated yield was calculated for the three steps starting from the aldehyde 6g. Light yellow oil (0.163 g, 48%). \( R_f \) (EtOAc/hexane 3:7) = 0.33. \([\alpha]_D^{22} = +39.3 \) (c 1.3 CHCl\(_3\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 1.66 (br s, 9H, C(CH\(_3\))\(_3\)), 2.76-2.92 (m, 2H, CH\(_2\)), 3.07-3.13 (m, 1H, CH), 3.81 (dd, 2H, \( J = 13.2, 13.5 \) Hz, CH\(_2\)Ph), 4.63-4.78 (m, 2H, CH\(_2\)), 4.95 (br s, 1H, CH), 5.93 (br dd, 1H, \( J = 1.2, 0.9 \) Hz, CH), 6.01 (d, 1H, \( J = 6.3 \) Hz, CH), 7.16-7.21 (br m, 5H, 5CH\(_{Ar}\)), 7.25-7.32 (m, 2H, 2CH\(_{Ar}\)), 7.44 (t, 2H, \( J = 12.6, 7.8 \) Hz, 2CH\(_{Ar}\)), 8.12 (br d, 1H, \( J = 13.2 \) Hz, CH\(_{Ar}\)). \(^{13}\)C\({}^1\)H NMR (75 MHz, CDCl\(_3\)) \( \delta \) 26.3, 28.2, 52.1, 60.0, 75.6, 83.3, 88.1, 115.2, 117.7, 119.1, 122.3, 123.6, 124.3, 126.7, 127.2, 127.9, 128.0, 128.2, 130.7, 135.5, 140.3, 149.6. IR (\( \nu_{\text{max}}/\text{cm}^{-1} \)) 3670 (w), 2978 (w), 2842 (w), 1729 (s), 1451 (s), 1367 (s), 1255 (s), 1155 (s), 1072 (s), 1015 (m), 935 (m), 856 (m), 743 (s), 697 (s). HRMS (ESI-TOF) \( m/z \) calcd for C\(_{26}\)H\(_{31}\)N\(_2\)O\(_3\) [M + H]\(^+\) 419.2335, found 419.2346.

**tert-Butyl** (S)-2-((R)-2,5-dihydrofuran-2-yl)pyrrolidine-1-carboxylate (25g). The allenyl precursor was prepared following the general procedure B using tert-butyl 2-formylpyrrolidine-1-carboxylate 6g (0.29 g, 1.45 mmol), allenylboronic acid pinacol ester 1 (0.36 mL, 1.89 mmol, 1.3 equiv.) and Et\(_2\)Zn (1 M in toluene, 156.3 \( \mu \)L, 0.145 mmol, 10 mol\%) in dry toluene (3 mL). Following the general procedure B the crude allenyl product was treated with AuPPh\(_3\)NTf\(_2\) (107.4 mg, 0.145 mmol, 10 mol\%) in dry dichloroethane (3 mL). The title compound 25g was obtained as a 1.6:1 mixture of syn and anti diastereomers after purification by flash column
chromatography (Et$_2$O/hexane 3:7). The isolated yield was calculated for the two steps starting from the aldehyde 6g. Colorless oil (0.21 g, 59%), $R_f$ (Et$_2$O/hexane 3:7) = 0.18. $^1$H NMR (500 MHz, DMSO, 80 °C) (mixture of two diastereomers, relative integrations given for each diastereomer) δ 1.41 (s, 9H, C(CH$_3$)$_3$, for each isomer), 1.70 (br s, 2H, 2CH$_2$, major isomer), 1.80-1.85 (m, 4H, 2CH$_2$, minor isomer) 3.14-3.22 (m, 2H, CH$_2$, major isomer), 3.31 (br s, 2H, CH$_2$, minor isomer), 3.75 (s, 1H, CH, major isomer), 3.90 (s, 1H, CH, minor isomer), 4.47-4.54 (m, 2H, CH$_2$, for each isomer), 4.97 (br s, 1H CH, for each isomer), 5.79-5.81 (m, 1H, CH=, for each isomer), 6.02 (br s, 1H, CH=, for each isomer). $^{13}$C{$^1$H} NMR (125 MHz, DMSO, 80 °C) (mixture of two diastereomers, minor indicated by asterisk) δ 23.9, 25.7, 28.61, 28.66*, 46.9*, 47.1, 59.7*, 60.6, 75.6, 78.7, 78.8*, 87.4, 127.2*, 128.0, 128.3, 128.4*, 154.0, 154.3*. IR ($v_{max}$/cm$^{-1}$) 2972 (m), 2878 (m), 2845 (m), 2355 (w), 1687 (s), 1456 (m), 1388 (s), 1363 (s), 1255 (m), 1165 (s), 1109 (s), 1072 (s), 769 (m), 678 (m).

HRMS (ESI-TOF) m/z calcd for C$_{13}$H$_{21}$NO$_3$Na [M + Na]$^+$ 262.1419, found 262.1427.

Acknowledgements

We thank the University of Wollongong for financial support of this research.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Determination of enantiomeric excess (ee) of oxazolidinones using (S)-10-camphorsulfonyl chloride 23a-c and 23f, chiral HPLC for determination of ee of aldehyde 2c and 6a and dihydrofuran 25a and NMR spectral data for all new substrates and for isolated products (PDF).
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