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

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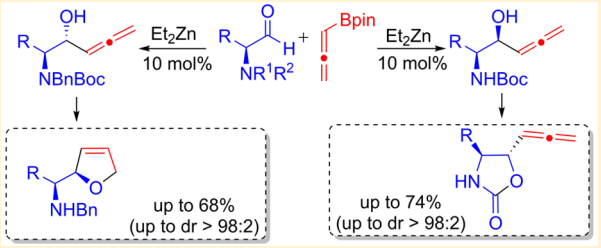
Supporting Information

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.

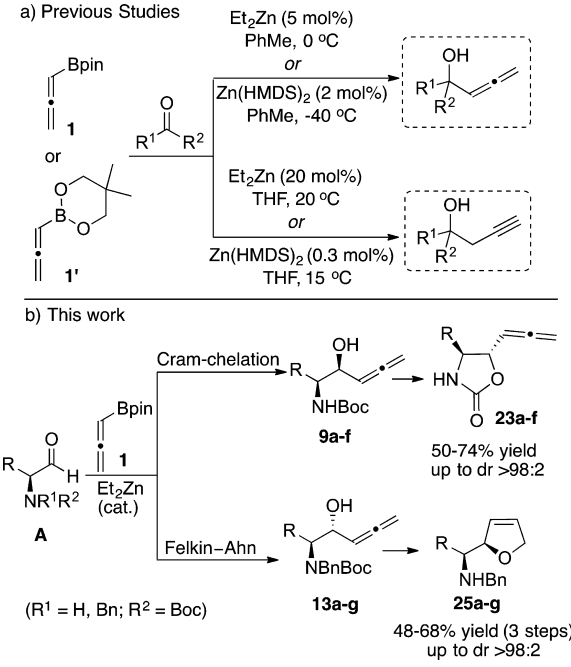


INTRODUCTION

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.[3]

A powerful route to allenes with a pendant O has been developed by Fandrick et al., who have demonstrated that Et_2Zn catalyzes the regioselective allenylation of various achiral aldehydes and ketones with allenylboronic acid pinacol ester **1** (Scheme 1a).[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.[4b] More recently, Kobayashi showed that a $Zn(HMDS)_2$ catalyzed process with allenylboronic acid 2,2-dimethyl-1,3-propanediol ester **1′** could also give either the allenyl or homopropargyl alcohols from the same starting materials by using kinetic or thermodynamic reaction control, respectively (Scheme 1a).[5] Despite these reports, methods to prepare allenes with multiple pendant heteroatoms are extremely rare[6] and mostly limited to systems containing only oxygen rather than both O and N; furthermore, the methods that do exist are not catalytic.[7] Combining both O and

Scheme 1. (a) Previous Methods for Preparing Allenylcarbinols from Allenylboronic Reagents 1 and 1′ Using Zinc Catalysts and (b) Current Study



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 α-amino aldehydes[8] (**A**, Scheme 1b) has not been developed, although the preparation of propargyl

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amino alcohols by the stoichiometric addition of propargylzinc species to α-amino aldehydes has been established.[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 Et_2Zn-catalyzed allenylation reactions of chiral α-amino aldehydes with allenylboronic acid pinacol ester **1**.

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.[10,11] Diastereoselective methods to prepare oxazolidinones with pendant unsaturated moieties are severely limited,[12] and whereas the preparation of 2,5-dihydrofurans by Au-catalyzed cyclization 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 multistep synthesis.[13]

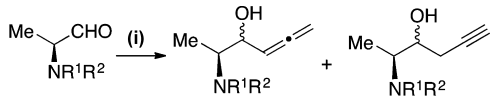
RESULTS AND DISCUSSION

The L-alanine-derived *N*-Boc-protected α-amino aldehyde **2a**[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 Et_2Zn as it is a commercially available and mild reagent unlikely to cause racemization of the α-amino aldehyde starting materials. When the reaction of allenyl boronate **1** and the aldehyde **2a** was conducted in toluene in the absence of Et_2Zn (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_2Zn 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 favor the propargyl product **16a** but with almost no diastereoselectivity (entry 3). The reaction also proceeded in CH_2Cl_2 but with modest regioselectivity (entry 4). An increase in the amount of catalyst from 5 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, whereas *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 we tested a range of singly *N*-protected α-amino alanals, *N,N*-diprotected α-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).[14] The reaction of the *N*-Bn and *N*-Boc alanal **6a** proved the most rewarding, giving the allenyl product **13** with good regioselectivity (89:11) and high diastereoselectivity (dr = 19:1 *anti*/*syn*).

The *anti* and *syn* configurations assigned to **9a** and **13a**, respectively, were based on ^1H 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.[6a] 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

Table 1. Optimization of Reaction Conditions[a]



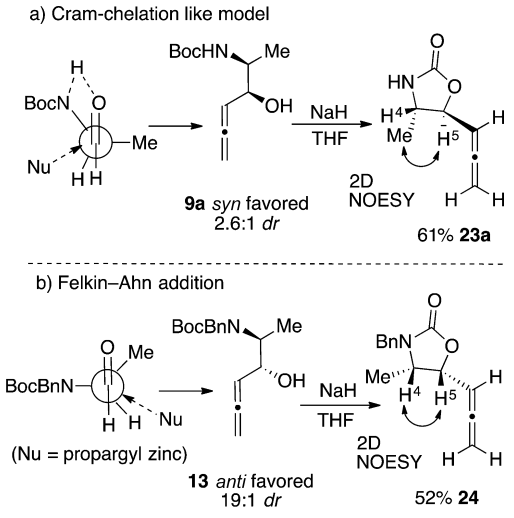
2a: R_1 = H, R_2 = Boc
3: R_1 = H, R_2 = Ts
4: R_1 = H, R_2 = Fmoc
5: R_1 = H, R_2 = Tr
6a: R_1 = Bn, R_2 = Boc
7: R_1 = Bn, R_2 = Ts
8: R_1 = Bn, R_2 = Bn

9a: R_1 = H, R_2 = Boc **16**
10: R_1 = H, R_2 = Ts **17**
11: R_1 = H, R_2 = Fmoc **18**
12: R_1 = H, R_2 = Tr **19**
13: R_1 = Bn, R_2 = Boc **20**
14: R_1 = Bn, R_2 = Ts **21**
15: R_1 = Bn, R_2 = Bn **22**

entry	NR^1R^2	sol.	cat. (mol %)	yield %,[b] (al/pr)[c]	dr[c] (*syn*/*anti*)
1	NHBoc	PhMe	0	12 (0:100)	2.6:1
2	NHBoc	PhMe	5	77 (97:3)	2.6:1
3	NHBoc	THF	5	60 (5:95)	1.1:1
4	NHBoc	CH_2Cl_2	5	38 (71:29)	2:1
5	**NHBoc**	**PhMe**	**10**	**92 (93:7)**	**2.6:1**
6	NHBoc[d]	PhMe	10	0	0
7	NHTs	PhMe	10	0[e]	0
8	NHFmoc	PhMe	10	0[f]	0
9	NHTr	PhMe	10	82 (84:16)	1.3:1
10	**NBnBoc**[g]	**PhMe**	**10**	**96 (89:11)**	**1:19**[h]
11	NBnTs[g]	PhMe	10	54[i] (94:6)	1:1.5
12	NBn_2[g]	PhMe	10	50[i] (94:6)	1:1.3

[a]Reaction conditions: (i) **1** (1.10 equiv), Et_2Zn, solvent, 0 °C, 18 h. [b]Isolated yield of allene and propargyl products. [c]Regioselectivity determined by ^1H 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]Recovery of SM. [g]With 1.3 equiv of **1**. [h]Determined by ^1H NMR analysis of *N*-Boc-deprotected crude RM. Decreasing the catalyst loading for this substrate resulted in incomplete conversion. [i]Isolated yield for the major allene diastereoisomer.

Scheme 2. Determination of Relative Configuration of the Allenyl Products



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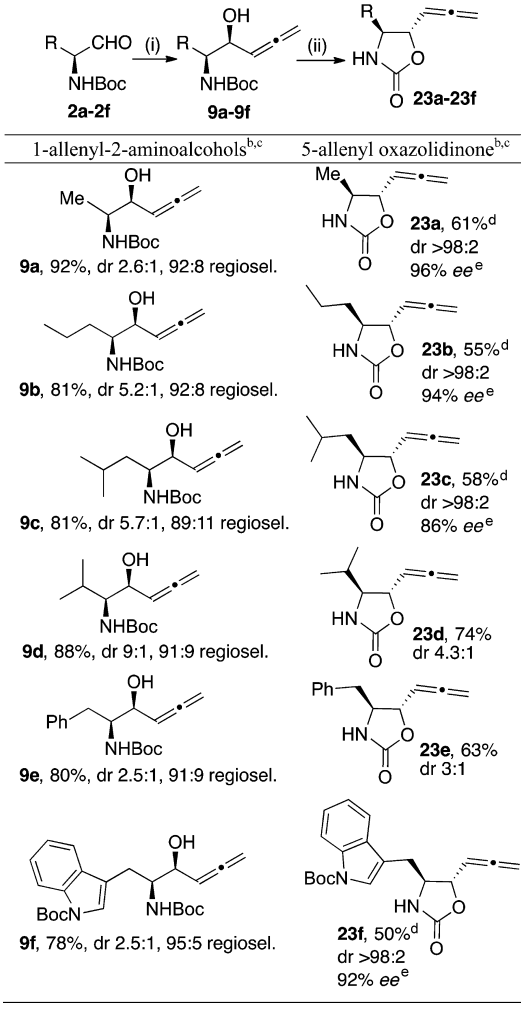
nucleophilic attack (Scheme 2a).[14e,f] Conversely, switching to the aldehyde having a more steric bulky, doubly protected nitrogen favors Felkin−Ahn control as H-bonding is no longer possible (Scheme 2b).[14a−d] That the dr for the uncatalyzed reaction (Table 1, entry 1) is identical to the catalyzed reaction provides further support for this H-bond model, rather than Zn playing a role in chelation.

Whereas only a moderate diastereoselectivity was observed for the allenylation of *N*-Boc-protected α-amino aldehyde **2a**, the reactions are highly regioselective. Furthermore, the levels of diastereoselectivity observed in Table 2 are comparable to those in the recently reported cross-benzoin condensation using *N*-Boc-protected α-amino aldehydes.[14d,e] 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[a]



[a]Reaction conditions: (i) **1** (1.1 equiv), Et_2Zn (10 mol %), toluene, 0 °C, 18 h; (ii) NaH (2 equiv), THF, rt, 1.5 h. [b]Isolated yield, with dr measured on purified oxazolidinone after chromatographic purification. [c]Regioselectivity and dr estimated by ^{1}H NMR analysis of purified **9**. [d]Isolated yield of the single major diastereomer. [e]Enantiomeric excess was determined by ^{1}H NMR analysis of the resulting diastereomeric (*S*)-camphorsulfonamide derivatives (see Supporting Information).

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,[15] which suggests they should be powerful synthetic intermediates for the synthesis of biologically 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 cyclizations 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 diastereomer using column chromatography, thus providing practical access to these intriguing heterocycles.[12,15]

We next explored the substrate scope of the allenylation reaction of the *N*-Bn and *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.[16] Consequently, following allenylation of aldehydes **6a−g** under the optimized conditions, a sequential Au(I)-catalyzed cyclization[17] 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 that with the purified material, expect for **25f**, which showed a dr of 4.9:1 in the crude reaction mixture, indicating that the minor diastereomer had been removed during purification. This method is advantageous for two reasons; first, the dihydrofurans are medicinally important skeletons, and second, 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 which are generally known for their propensity for racemization.[8] Therefore, the enantiorretention of representative reactions from Table 2 and Table 3 was investigated, and gratifyingly, no erosion of enantiopurity was observed in any case. The enantiomeric excesses of diastereomerically enriched oxazolidinones **23a−c** and **23f** were

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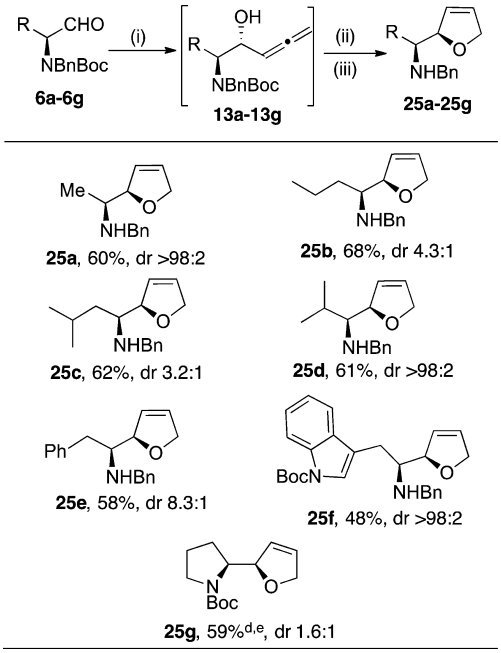
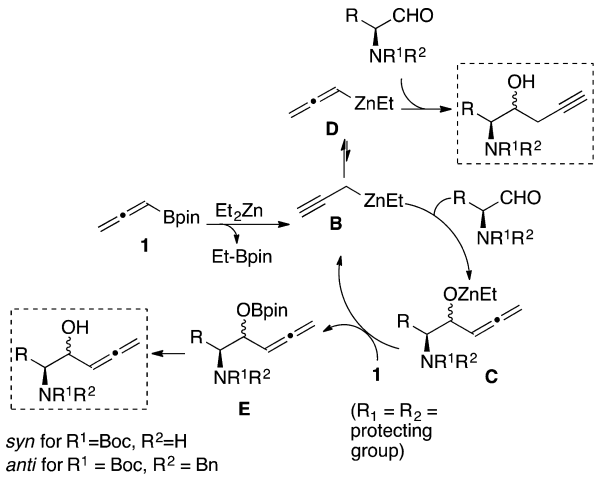
Table 3. Reaction Scope of 2,5-Dihydrofurans[a,b,c]



[a]Reaction conditions: (i) **1** (1.3 equiv), Et_2Zn (10 mol %), PhMe, 0 °C, 18 h; (ii) $AuPPh_3NTf_2$ (10 mol %), DCE, 60 °C, 8 h; (iii) TMSCl (5 equiv), MeOH, rt, overnight. [b]Isolated yields over three steps without any intermediate purification. [c]Diastereoselectivity determined by ^1H NMR analysis of purified **25**. [d]The *N*-Boc-deprotected product could not be obtained due to instability. [e]Isolated yield from two steps.

Scheme 3. Proposed Catalytic Cycle for the Zn-Catalyzed Allenylation Reactions



determined by preparation of their (*S*)-camphorsulfonyl derivatives according to the previously reported method[20] (see Supporting Information). The enantiomeric excesses of **23a** (96% ee) and **23c** (86% ee) were identical to those of their precursor aldehydes **2a** (96% ee)[8] and **2c** (86% ee), 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 Supporting Information). However, this method was not suitable for the 2,5-dihydrofuran products **25** due to instability of the corresponding camphorsulfonyl derivative. Therefore, the enantiomeric excess of the precursor aldehyde **6a** (91% ee) was determined by chiral HPLC (see Supporting Information), which was identical to that of its derived dihydrofuran **25a** (91% ee, from chiral HPLC analysis; see Supporting Information).

The proposed mechanism for these allenylation reactions is shown in Scheme 3 and is consistent with the proposal of Fandrick and co-workers.[4] Transmetalation between **1** and Et_2Zn gives the reactive propargylic Zn species **B**, which under the kinetic control conditions of the reaction reacts in an S_E2' 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**.

It is also possible that Et_2Zn is regenerated by reaction of the alkoxide **C** with EtBpin generated in the initial transmetalation. Isomerization 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, whereas 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 enantioselectivity 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 allenyloxazoldinone 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 4 Å molecular sieves. All reactions using air/moisture-sensitive reagents were performed in oven-dried glassware, under an atmosphere of nitrogen equipped with a stir bar. Reactions were monitored by thin-layer chromatography (TLC) on aluminum-backed silica gel sheets, visualized with UV light (254 nm) fluorescence quenching, followed by staining of the plates with potassium permanganate. Column chromatography used for compound purification was performed using prepacked flash grade silica gel (40–75 nm) as the stationary phase. ^1H NMR and $^{13}C\{^1H\}$ NMR spectra were recorded either at 300, 400, and 500 MHz for ^1H NMR or at 75, 100, and 125 MHz for ^{13}C NMR. All ^1H NMR and $^{13}C\{^1H\}$ 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 and were corrected to 0.00 ppm (TMS) for ^1H NMR and 77.00 ppm ($CDCl_3$ center line) for ^{13}C NMR. The α-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 details below).

Synthesis of Singly *N*-Protected Amino Aldehydes. The *N*-protected α-amino aldehydes **2a**,[21a] **2c**,[21b] **2d**,[21c] **2e**,[21d] **3**,[21e] **4**,[21f] and

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5[21g] are known and were prepared by the previously reported methods.

Methyl (*S*)-*tert*-Butyl(1-oxopentan-2-yl)carbamate (2b). *Methyl 2-((tert-Butoxycarbonyl)amino)pentanoate **S1**.* To a solution of methyl 2-aminopentanoate hydrochloride[22a] (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 $NaHCO_3$ solution and the separated organic layer washed with brine solution and dried over Na_2SO_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 have not been published so are included here.[23] R_f (Et_2O/hexane 2:8) = 0.42. $[\alpha]_D^{22}$ = +84.6 (*c* 2, $CHCl_3$). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 13.5, 18.5, 28.1, 34.6, 52.0, 53.1, 79.5, 155.3, 173.4. IR (ν_{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 $C_{11}H_{21}NO_4Na$ $[M + Na]^+$ 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_2SO_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)-1*H*-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[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)-1*H*-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.[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)-1*H*-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). $[\alpha]_D^{22}$ = +53.5 (*c* 3.2, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.44 (s, 9H, $C(CH_3)_3$), 1.66 (s, 9H, $C(CH_3)_3$), 3.22 (br s, 2H, CH_2Ph), 4.48 (br s, 1H, C*H*), 5.22 (br s, 1H, N*H*), 7.25 (br s, 1H, CH_{Ar}), 7.32 (br s, 1H, CH_{Ar}), 7.43 (br s, 1H, CH_{Ar}), 7.54 (br s, 1H, CH_{Ar}), 8.13 (br s, 1H, CH_{Ar}), 9.65 (s, 1H, CHO). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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 (ν_{max}/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 $C_{21}H_{28}N_2O_5Na$ $[M + Na]^+$ 411.1896, found 411.1878.

Preparation of Doubly Protected α-Amino Esters and Aldehydes. The *N*-Bn,*N*-Boc α-amino aldehyde **6e**[26] and the *N*-Boc α-amino prolinal **6g**,[27] *N*-Bn,*N*-Ts α-amino alaninal **7**,[28] and *N*,*N*-dibenzyl-α-amino alaninal **8**[29] 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,[21e] (*S*)-*tert*-butyl benzyl(1-hydroxypropan-2-yl)carbamate,[30a] (*S*)-methyl *N*-benzyl valinate,[31a] and (*S*)-2-(benzylamino)-3-methylbutan-1-ol[31b] 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[30a] (0.42 g, 1.58 mmol) in CH_2Cl_2 (30 mL) at 0 °C were added saturated aqueous $NaHCO_3$ 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 $Na_2S_2O_3$ solution (15 mL) and extracted into CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) 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 enantioselectivity was determined by chiral HPLC analysis of the corresponding alcohol (obtained by $NaBH_4$ reduction of a small quantity of the unpurified aldehyde) using a Phenomenex Lux i-Cellulose-5 column; hexane/isopropyl alcohol (95:5); flow rate = 0.5 mL/min; 210 nm; t_{major} = 23.29 min, t_{minor} = 25.15 min, 91% ee. The data match that previously reported.[30b]

(*S*)-*tert*-Butyl Benzyl(1-oxopentan-2-yl)carbamate (6b). *Methyl 2-(Benzylamino)pentanoate **S3**.* To a stirred suspension of L-norvaline methyl ester hydrochloride[22a] (1.30 g, 7.75 mmol) and benzyl bromide (0.90 mL, 7.75 mmol, 1.0 equiv) in acetonitrile (20 mL) was added potassium carbonate (2.14 g, 15.50 mmol, 2.0 equiv), and the mixture was stirred overnight at room temperature. The reaction mixture was washed with saturated aqueous NH_4Cl solution (30 mL) and water (30 mL), dried ($MgSO_4$), concentrated under reduced pressure, and purified by flash column chromatography (Et_2O/hexane 1:9) to obtain the *N*-benzylated product **S3**. Colorless oil (1.25 g, 73%). R_f (Et_2O/hexane 1:9) = 0.16. $[\alpha]_D^{22}$ = −35.4 (*c* 5.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J* = 7.2 Hz, CH_3), 1.33−1.43 (m, 2H, CH_2), 1.57−1.64 (m, 2H, CH_2), 1.79 (s, 1H, N*H*), 3.26 (t, 1H, *J* = 6.6 Hz, C*H*), 3.61 (d, 1H, *J* = 13.2 Hz, C*H*Ph), 3.67 (s, 3H, CH_3), 3.80 (d, 1H, *J* = 12.9 Hz, C*H*Ph), 7.22−7.31 (m, 5H, $5CH_{Ar}$). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 13.8, 19.0, 35.7, 51.5, 52.1, 60.5, 126.9, 128.2, 128.3, 139.9, 176.0. IR (ν_{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.

*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_2O, 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 (1 M, 15 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification was carried out by flash column chromatography (Et_2O/hexane 1:9) to yield the *N*-Bn,*N*-Boc α-amino ester **S6**. Colorless oil (0.89 g, 62%). R_f (Et_2O/hexane 1:9) = 0.23. $[\alpha]_D^{22}$ = −50.4 (*c* 9.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of rotamers): δ 0.79 (br s, 3H, CH_3), 1.24 (br s, 2H, CH_2), 1.40 (br s, 4.2H, $C(CH_3)_3$), 1.45 (br s, 4.8H, $C(CH_3)_3$), 1.62−1.75 (m, 1H, C*H*), 1.84−1.94 (m, 1H, C*H*), 3.55 (s, 3H, CH_3), 3.90−4.80 (m, 3H, CH_2Ph, C*H*), 7.19−7.28 (m, 5H, $5CH_{Ar}$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) (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 (ν_{max}/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 $C_{18}H_{27}NO_4Na$ $[M + Na]^+$ 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

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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%). R_f (EtOAc/hexane 4:6) = 0.61. $[\alpha]_D^{22}$ = +16.3 (*c* 4.6, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) (mixture of rotamers): δ 0.84 (br s, 3H, CH_3), 1.26 (br s, 2H, CH_2), 1.37 (br s, 7H, $C(CH_3)_3$, *CH*), 1.49 (br s, 4H, $C(CH_3)_3$, *CH*), 3.40−3.60 (m, 3H), 3.84−3.86 (m, 1H, *CH*), 4.21−4.70 (m, 2H, CH_2Ph), 7.21−7.27 (m, 5H, $5CH_{Ar}$). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) (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 (ν_{max}/cm^{-1}) 3446 (m), 2959 (m), 2930 (m), 2873 (m), 1665 (s), 1465 (m), 1410 (s), 1341 (m), 1243 (m), 1166 (s), 1053 (w), 701 (s). HRMS (ESI-TOF) *m*/*z* calcd for $C_{17}H_{27}NO_3Na$ $[M + Na]^+$ 316.1889, found 316.1891.

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 Et_3N (4.56 mL, 32.17 mmol, 16 equiv) in CH_2Cl_2 (5 mL) at −78 °C. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (5 mL) and extracted into CH_2Cl_2 (3 × 3 mL). The combined organic layers were washed with brine solution (10 mL), dried (Na_2SO_4), 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 dimethylsulfoxide can react explosively at room temperature. Furthermore, this procedure should be carried out in a fumehood because dimethylsulfide is an odorous byproduct of the reaction.[32]) R_f (EtOAc/hexane 1:9) = 0.43. $[\alpha]_D^{22}$ = −92.3 (*c* 7.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of rotamers): δ 0.89 (t, 3H, *J* = 7.2 Hz, CH_3), 1.34−1.41 (m, 2H, CH_2), 1.45 (br s, 9H, $C(CH_3)_3$), 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, *CH*Ph), 4.70 (br d, 0.4H, *J* = 15.0 Hz, *CH*Ph), 4.98 (br d, 0.6H, *J* = 15.0 Hz, *CH*Ph), 7.26−7.35 (m, 5H, $5CH_{Ar}$), 9.35 (br s, 0.6H, *CH*O), 9.44 (br s, 0.4H, *CH*O). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) (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 (ν_{max}/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 $C_{17}H_{25}NO_3Na$ $[M + Na]^+$ 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_4Cl solution (20 mL) and water (20 mL), dried ($MgSO_4$), concentrated under reduced pressure, and purified by flash column chromatography (Et_2O/hexane 1:9) to obtain the *N*-benzylated product **S6**. Light yellow oil (0.996 g, 77%). Data match 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_2O, 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 (1 M, 5 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification was carried out by flash column chromatography (Et_2O/hexane 1:9) to yield the *N*-Bn,*N*-Boc α-amino ester **S7**. Colorless oil (0.59 g, 70%). Data match 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 °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_2SO_4) and concentrated under reduced pressure to yield the desired aldehyde. Colorless oil (0.35 g, 65%). Data match 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_2O, 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 (1 M, 15 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification was carried out by flash column chromatography (Et_2O/hexane 1:9) to yield the *N*-Bn,*N*-Boc α-amino ester **S8**. Colorless oil (1.18 g, 63%). Data match 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-(benzylamino)-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_3N (5.63 mL, 39.68 mmol, 16 equiv) in CH_2Cl_2 (5 mL) at −78 °C. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (5 mL) and extracted into CH_2Cl_2 (3 × 3 mL). The combined organic layers were washed with brine solution (10 mL), dried (Na_2SO_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 match that reported previously.[31b]

(*S*)-*tert*-Butyl 3-(2-(Benzyl(*tert*-butoxycarbonyl)amino)-3-oxopropyl)-1*H*-indole-1-carboxylate (6f). *Methyl Benzyl-L-tryptophanate* ***S9***. Methyl tryptophanate hydrochloride[22b] (3.60 g, 14.13 mmol) was neutralized into the free base by being dissolved in diethyl ether (20 mL), followed by treatment with saturated aqueous K_2CO_3 solution (20 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to obtain a light yellow oil. To a stirred suspension of neutralized tryptophan methyl ester and $MgSO_4$ (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 $NaBH_4$ (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 NH_4OH (5%, 20 mL), extracted by ethyl acetate, and dried (Na_2SO_4). 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 match that reported previously.[22b]

Methyl N^{α}-Benzyl-N^{α}-(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 match 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 N^{α}-benzyl-N^{α}-(*tert*-butoxycarbonyl)-L-tryptophanate **S10** (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), saturated aqueous $NaHCO_3$ solution (30 mL), and brine (30 mL). The organic layer was dried (Na_2SO_4), and the filtrate was concentrated under reduced pressure. The title compound **S11** was

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obtained after flash column chromatography (EtOAc/hexane 2:9) as a colorless gummy oil (1.15 g, 86%). R_f (EtOAc/hexane 2:9) = 0.48. $[\alpha]_D^{22}$ = −67.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of rotamers): δ 1.48 (s, 9H, $3CH_3$), 1.65 (s, 9H, $3CH_3$), 3.10−3.39 (m, 2H, CH_2), 3.62 (s, 3H, CH_3), 4.15−4.39 (m, 3H, CH_2, *CH*), 7.01−7.42 (m, 9H, $9CH_{Ar}$), 8.11 (br d, 1H, *J* = 6.9 Hz, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of rotamers, minor rotamer indicated by asterisk): δ 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 (ν_{max}/cm^{-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 $C_{29}H_{36}N_2O_6Na$ $[M + Na]^+$ 531.2471, found 531.2492.

tert-Butyl (*S*)-3-(2-(*N*-Benzylformamido)-3-methoxy-3-oxopropyl)-1*H*-indole-1-carboxylate **6f**. To a solution of *tert*-butyl 3-(2-(benzyl(*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)-1*H*-indole-1-carboxylate **S11** (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_2SO_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. $[\alpha]_D^{22}$ = −113.5 (*c* 9.8, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) (mixture of rotamers): δ 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, *CH*Ph), 4.50 (d, 0.5H, *J* = 15.0 Hz, *CH*Ph), 4.76 (d, 0.5H, *J* = 15.0 Hz, *CH*Ph), 7.00 (br s, 2H, $2CH_{Ar}$), 7.19−7.24 (m, 4H, $4CH_{Ar}$), 7.31−7.41 (m, 3H, $3CH_{Ar}$), 8.16 (br s, 1H, CH_{Ar}), 9.42 (s, 0.5H, *CH*O), 9.53 (0.5H, *CH*O). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) (mixture of rotamers, minor rotamer indicated by asterisk): δ 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 (ν_{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 $C_{28}H_{33}N_2O_5$ $[M - H]^+$ 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 NH_4Cl solution (50 mL) and water (50 mL), dried ($MgSO_4$), 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%). R_f (EtOAc/hexane 3:7) = 0.54. $[\alpha]_D^{22}$ = −42.5 (*c* 2.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.26−1.28 (m, 3H, CH_3), 2.42 (br s, 3H, CH_3), 3.42 (br s, 3H, CH_3), 4.42 (br d, 1H, *J* = 14.5 Hz, *CH*Ph), 4.55 (br d, 1H, *J* = 16.0 Hz, *CH*Ph), 4.61−4.63 (m, 1H, *CH*), 7.23−7.32 (m, 7H, $7CH_{Ar}$), 7.71 (br d, 2H, *J* = 5.5 Hz, $2CH_{Ar}$). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 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 (ν_{max}/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 $C_{18}H_{21}NO_4NaS$ $[M + Na]^+$ 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 Et_2Zn (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 NH_4Cl solution, and washed with saturated aqueous $NaHCO_3$ solution (15 mL) and water (10 mL). The organic layer was dried (Na_2SO_4), 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 NH_4Cl solution, washed with water (10 mL), dried ($MgSO_4$), and then purified by flash column chromatography (acetone/*n*-pentane) to afford the corresponding oxazolidinone products **23a**−**23f**.

***tert*-Butyl ((2*S*,3*S*)-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 Et_2Zn (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. ^{1}H NMR (500 MHz, $CDCl_3$) (mixture of two allene diastereomers, relative integrations given for each diastereomer): δ 1.12 (d, 3H, *J* = 6.5 Hz, CH_3, minor isomer), 1.19 (d, 3H, *J* = 7.0 Hz, CH_3, major isomer), 1.44 (s, 9H, $C(CH_3)_3$, for each isomer), 2.87 (br s, 1H, O*H*, major isomer), 3.17 (br s, 1H, O*H*, minor isomer), 3.71−3.75 (m, 1H, C*H*, major isomer), 3.75−3.82 (m, 1H, C*H*, minor isomer), 4.09 (br s, 1H, C*H*, major isomer), 4.23 (br s, 1H, C*H*, minor isomer), 4.86−4.90 (m, 2H, CH_2=C=, for each isomer), 5.16−5.28 (m, 1H, *CH*=C=, for each isomer). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) (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), 1955 (w), 1683 (s), 1506 (m), 1365 (m), 1257 (m), 1162 (s), 1051 (s), 1024 (s). HRMS (ESI-TOF) *m*/*z* calcd for $C_{11}H_{18}NO_3$ $[M - H]^+$ 212.1287, found 212.1289.

(4*S*,5*S*)-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_f (2% CH_2Cl_2/Et_2O) = 0.52. $[\alpha]_D^{22}$ = −30.3 (*c* 1.2, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.28 (d, 3H, *J* = 6.0 Hz, CH_3), 3.75−3.80 (m, 1H, C*H*), 4.55 (t, 1H, *J* = 6.5, 7.0 Hz, C*H*), 4.93−5.00 (m, 2H, CH_2=C=), 5.32 (q, 1H, *J* = 7.0 Hz, *CH*=C=), 6.02 (br s, 1H, N*H*). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 20.0, 54.0, 78.6, 81.6, 89.0, 158.9, 209.2. IR (ν_{max}/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 $C_7H_9NO_2Na$ $[M + Na]^+$ 162.0531, found 162.0537.

***tert*-Butyl ((4*S*,5*S*)-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 Et_2Zn (1 M in toluene, 79.17 μL, 0.074 mmol, 10 mol %) in dry toluene (2 mL). Colorless oil (0.145 g, 81%). R_f (EtOAc/hexane 2:8) = 0.45. ^{1}H NMR (500 MHz, $CDCl_3$) (mixture of two allene diastereomers, relative integrations given for each diastereomer): δ 0.92 (t, 3H, *J* = 7.0 Hz, CH_3, for each isomer), 1.31−1.40 (m, 3H, *CH* and CH_2, for each isomer), 1.43 (s, 9H, $C(CH_3)_3$, for each isomer), 1.50−1.56 (m, H, C*H*, for each isomer), 3.00 (br s, 1H, O*H*, minor isomer), 3.17 (br s, 1H, O*H*, major isomer), 3.59 (br s, 1H, C*H*, major isomer), 3.70−3.73 (m, 1H, C*H*, minor isomer), 4.16 (br s, 1H, C*H*, major isomer), 4.23 (br s, 1H, C*H*, minor isomer), 4.85−4.90 (m, 2H, CH_2=C=, major isomer), 4.94−4.96 (m, 2H, CH_2=C=, minor isomer), 5.18−5.27 (m, 1H, *CH*=C=, for each isomer). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) (mixture of two allene diastereomers, minor indicated by asterisk): δ 13.9, 19.3, 28.3, 34.0, 34.2*, 54.9, 55.2*,

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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), 1506 (s), 1365 (s), 1248 (s), 1166 (s), 1055 (s), 1018 (s), 843 (s). HRMS (ESI-TOF) m/z calcd for $C_{13}H_{23}NO_3Na$ $[M + Na]^+$ 264.1576, found 264.1573.

(4*S*,5*S*)-5-(Propa-1,2-dien-1-yl)-4-propyloxazolidin-2-one (23b). The title compound **23b** was obtained as s 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. $[\alpha]_D^{22}$ = −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, CH_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, C*H*), 4.62−4.65 (m, 1H, C*H*), 4.96−4.99 (m, 2H, CH_2═C═), 5.34 (q, 1H, *J* = 6.5, 7.0 Hz, C*H*═C═), 6.51 (br s, 1H, N*H*). ^{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 $C_9H_{12}NO_2$ $[M - H]^+$ 166.0862, found 166.0870.

***tert*-Butyl ((4*S*,5*S*)-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_2Zn (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): δ 0.92 (d, 6H, *J* = 6.0 Hz, $2CH_3$, for each isomer), 1.27−1.39 (m, 1H, C*H*, 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, O*H*, major isomer), 2.95 (br s, 1H, O*H*, minor isomer), 3.68 (br s, 1H, C*H*, major isomer), 3.70−3.80 (br s, 1H, C*H*, minor isomer), 4.12 (br s, 1H, C*H*, major isomer), 4.22 (br s, 1H, C*H*, minor isomer), 4.79−4.90 (m, 2H, CH_2═C═, for each isomer), 5.18−5.20 (m, 1H, C*H*═C═, minor isomer), 5.25−5.27 (m, 1H, C*H*═C═, major isomer). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) (mixture of two allene diastereomers, minor indicated by asterisk): δ 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 (ν_{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 $C_{14}H_{25}NO_3Na$ $[M + Na]^+$ 278.1732, found 278.1720.

(4*S*,5*S*)-4-Isobutyl-5-(propa-1,2-dien-1-yl)oxazolidin-2-one (23c). The title compound **23c** was obtained as s 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, $CDCl_3$): δ 0.91−0.93 (m, 6H, $2CH_3$), 1.38−1.43 (m, 1H, C*H*), 1.48−1.53 (m, 1H, C*H*), 1.61−1.68 (m, 1H, C*H*), 3.70−3.74 (m, 1H, C*H*), 4.58−4.61 (m, 1H, C*H*), 4.93−5.00 (m, 2H, CH_2═C═), 5.33 (q, 1H, *J* = 6.5 Hz, C*H*═C═), 6.28 (br s, 1H, N*H*). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 22.2, 23.1, 25.2, 44.1, 56.5, 78.6, 80.5, 89.5, 159.1, 209.1. IR (ν_{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 $C_{10}H_{15}NO_2Na$ $[M + Na]^+$ 204.0995, found 204.0996.

***tert*-Butyl ((3*S*,4*S*)-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 Et_2Zn (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. R_f (EtOAc/hexane 2:8) = 0.35. ^{1}H NMR (500 MHz, $CDCl_3$) (mixture of two allene diastereomers, relative integrations given for each diastereomer): δ 0.94 (d, 3H, *J* = 6.5 Hz, CH_3, for each isomer), 0.99 (d, 3H, *J* = 6.5 Hz, CH_3, for each isomer), 1.44 (s, 9H, $C(CH_3)_3$, for each isomer), 1.87−1.93 (m, 1H, C*H*, for each isomer), 2.68 (br s, 1H, O*H*, minor isomer), 2.80 (br s, 1H, O*H*, major isomer), 3.20−3.23 (m, 1H, C*H*, minor isomer), 3.26−3.29 (m, 1H, C*H*, major isomer), 4.28 (br s, 1H, C*H*, minor isomer), 4.33 (br s, 1H, C*H*, major isomer), 4.85−4.93 (m, 2H, CH_2═C═, for each isomer), 5.19−5.21 (m, 1H, C*H*═C═, minor isomer), 5.25−5.26 (m, 1H, C*H*═C═, major isomer). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) (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}) 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 $C_{13}H_{23}NO_3Na$ $[M + Na]^+$ 264.1576, found 264.1581.

(4*S*,5*S*)-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%). R_f (acetone/*n*-pentane 2:8) = 0.44. ^{1}H NMR (500 MHz, $CDCl_3$) (mixture of two diastereomers, relative integrations given for each diastereomer): δ 0.94 (br d, 3H, *J* = 6.5 Hz, CH_3, major isomer), 0.98 (br d, 3H, *J* = 6.0 Hz, CH_3, major isomer), 0.99 (br d, 3H, *J* = 6.0 Hz, CH_3, minor isomer), 1.77 (br s, 1H, C*H*, major isomer), 1.90 (br s, 1H, C*H*, minor isomer), 3.45 (br s, 1H, C*H*, major isomer), 3.61−3.63 (m, 1H, C*H*, major isomer), 4.74 (br s, 1H, C*H*, major isomer), 4.92−4.97 (m, 2H, CH_2═C═, for each isomer), 5.04−5.06 (m, 1H, C*H*, minor isomer), 5.32−5.37 (m, 1H, C*H*═C═, for each isomer), 6.58 (br s, 1H, N*H*, minor isomer), 6.66 (br s, 1H, N*H*, major isomer). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) (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 (ν_{max}/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 $C_9H_{13}NO_2Na$ $[M + Na]^+$ 190.0838, found 190.0840.

***tert*-Butyl ((2*S*,3*S*)-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 Et_2Zn (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. R_f (EtOAc/hexane 3:7) = 0.53. ^{1}H NMR (500 MHz, $CDCl_3$) (mixture of two allene diastereomers, relative integrations given for each diastereomer): δ 1.36 (s, 9H, $C(CH_3)_3$, minor isomer), 1.43 (s, 9H, $C(CH_3)_3$, major isomer), 2.61 (br s, 1H, O*H*, major isomer), 2.88−2.96 (m, 2H, CH_2Ph, for each isomer), 3.76 (br s, 1H, C*H*, minor isomer), 3.82 (br s, 1H, C*H*, major isomer), 4.15 (br s, 1H, C*H*, major isomer), 4.27 (br s, 1H, C*H*, minor isomer), 4.85−4.91 (m, 2H, CH_2═C═, for each isomer), 5.24−5.29 (m, 1H, C*H*═C═, for each isomer), 7.19−7.29 (m, 5H, $5CH_{Ar}$, for each isomer). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) (mixture of two allene diastereomers, minor indicated by asterisk): δ 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 (ν_{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.

(4*S*,5*S*)-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): δ 2.70−2.75 (m, 2H, CH_2Ph, minor isomer), 2.86−2.90 (m, 2H, CH_2Ph,

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major isomer), 3.90 (q, 1H, J = 6.5 Hz, C*H*, major isomer), 4.10−4.14 (m, 1H, C*H*, minor isomer), 4.72 (t, 1H, J = 6.0 Hz, C*H*, 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, C*H*, minor isomer), 5.24 (q, 1H, J = 6.5, 7.0 Hz, C*H*=C=, major isomer), 5.35 (q, 1H, J = 7.0 Hz, C*H*=C=, minor isomer), 5.65 (br s, 1H, N*H*, minor isomer), 6.19 (br s, 1H, N*H*, 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). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) (mixture of two diastereomers, minor indicated by asterisk): δ 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 (ν_{max}/cm^{-1}) 3267 (w), 2917 (w), 1955 (w), 1743 (s), 1386 (m), 1230 (m), 992 (s), 854 (s), 699 (s). HRMS (ESI-TOF) m/z calcd for $C_{13}H_{13}NO_2Na$ $[M + Na]^+$ 238.0838, found 238.0840.

***tert*-Butyl 3-((2*S*,3*S*)-2-((*tert*-Butoxycarbonyl)amino)-3-hydroxyhexa-4,5-dien-1-yl)-1*H*-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)-1*H*-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_2Zn (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. ^1H NMR (500 MHz, $CDCl_3$) (mixture of two allene diastereomers, relative integrations given for each diastereomer): δ 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, C*H*, major isomer), 4.06 (br s, 1H, C*H*, minor isomer), 4.23 (br s, 1H, C*H*, major isomer), 4.32 (br s, 1H, C*H*, minor isomer), 4.87−5.04 (m, 2H, CH_2=C=, for each isomer), 5.26−5.32 (m, 1H, C*H*=C=, for each isomer), 7.22−7.66 (m, 4H, 4CH_{Ar}, for each isomer), 8.13 (br s, 1H, CH_{Ar}, for each isomer). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) (mixture of two allene diastereomers, minor indicated by asterisk): δ 28.2, 28.3*, 54.7, 55.3*, 69.3, 71.7*, 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_{max}/cm^{-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 $C_{24}H_{32}N_2O_5Na$ $[M + Na]^+$ 451.2209, found 451.2227.

***tert*-Butyl 3-(((4*R*,5*R*)-2-Oxo-5-(propa-1,2-dien-1-yl)-oxazolidin-4-yl)methyl)-1*H*-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_f (acetone/*n*-pentane 2:8) = 0.26. $[\alpha]_D^{22}$ = −35.8 (c 0.7, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 1.68 (s, 9H, C(CH_3)$_3$), 2.90−2.94 (m, 1H, C*H*), 3.00−3.04 (m, 1H, C*H*), 4.03 (br s, 1H, C*H*), 4.81 (br s, 1H, C*H*), 4.96 (br s, 2H, CH_2=C=), 5.19 (br s, 1H, N*H*), 5.37 (br d, 1H, J = 6.5 Hz, C*H*=C=), 7.26 (br s, 1H, CH_{Ar}), 7.34−7.37 (m, 1H, CH_{Ar}), 7.46 (br s, 2H, 2CH_{Ar}), 8.15 (br s, 1H, CH_{Ar}). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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_{max}/cm^{-1}) 3277 (w), 2982 (w), 2357 (w), 1955 (w), 1751 (s), 1730 (s), 1452 (s), 1368 (s), 1255 (s), 1155 (s), 1086 (m), 854 (m). HRMS (ESI-TOF) m/z calcd for $C_{20}H_{23}N_2O_4$ $[M + H]^+$ 355.1658, found 355.1664.

(2*S*,3*S*)-2-(Tritylamino)hexa-4,5-dien-3-ol (12). The title compound **12** was obtained after flash column chromatography (Et_2O/hexane 2:8) as a 1.3:1 mixture of *syn* and *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 Et_2Zn (1 M in toluene, 34.0 μL, 0.0317 mmol, 10 mol %) in dry toluene (1 mL). Colorless oil (0.093 g, 82%). R_f (Et_2O/hexane 2:8) = 0.41. ^1H NMR (300 MHz, $CDCl_3$) (mixture of two allene diastereomers, relative integrations given for each diastereomer): δ 0.43 (d, 3H, J = 6.0 Hz, CH_3, minor isomer), 0.75 (d, 3H, J = 6.6 Hz, CH_3, major isomer), 2.23 (br s, 1H, N*H*, for each isomer), 2.69−2.77 (m, 1H, C*H*, for each isomer), 3.40−3.43 (m, 1H, C*H*, for each isomer), 4.74−4.77 (m, 2H, CH_2=C, major isomer), 4.80−4.83 (m, 2H, CH_2=C, minor isomer), 4.98 (q, 1H, J = 6.0, 6.3 Hz, C*H*=C, major isomer), 5.22 (q, 1H, J = 6.6, 6.6 Hz, C*H*=C, minor isomer), 7.15−7.28 (m, 10H, 10CH_{Ar}, for each isomer), 7.54 (d, 5H, J = 7.8 Hz, 5CH_{Ar}, for each isomer). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) (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 (ν_{max}/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 $C_{25}H_{26}NO$ $[M + H]^+$ 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 Et_2Zn (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 NH_4Cl solution (5 mL) and then washed with saturated aqueous $NaHCO_3$ solution (15 mL) and water (10 mL). The organic layer was dried (Na_2SO_4) 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 $AuPPh_3NTf_2$ (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 $NaHCO_3$ 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((2*S*,3*R*)-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 Et_2Zn (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. $[\alpha]_D^{22}$ = +7.31 (c 7.2, CH_3Cl). ^1H NMR (500 MHz, $CDCl_3$) (mixture of rotamers): δ 1.17 (d, 0.7H, J = 7.0 Hz), 1.20 (d, 2.3H, J = 7.0 Hz), 1.33−1.45 (br s, 9H, C(CH_3)$_3$), 3.70−3.76 (m, 1H, C*H*), 4.01−4.12 (m, 0.7H), 4.35−4.49 (m, 3.3H), 4.80 (m, 2H, CH_2=C=), 5.12−5.17 (m, 1H, C*H*=C=), 7.23−7.33 (m, 5H, 5CH_{Ar}). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) (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. IR (ν_{max}/cm^{-1}) 3473 (m), 2976 (m), 1956 (m), 1680 (s), 1452 (s), 1365 (s), 1332 (m), 1250 (m), 1164 (s), 1012 (s), 860 (s), 699 (s). HRMS (ESI-TOF) m/z calcd for $C_{18}H_{25}NO_3Na$ $[M + Na]^+$ 326.1721, found 326.1731.

***N*-Benzyl-*N*-((2*S*,3*R*)-3-hydroxyhexa-4,5-dien-2-yl)-4-methylbenzenesulfonamide (14).** The major diastereomer of the title compound **14** was obtained after purification by flash column chromatography (EtOAc/hexane 3:7) following the first part of general procedure B using *N*-benzyl-4-methyl-*N*-(1-oxopropan-2-yl)benzenesulfonamide **7** (0.072 g, 0.226 mmol), allenylboronic acid pinacol ester **1** (56.50 μL, 0.29 mmol, 1.3 equiv), and Et_2Zn (1 M in toluene, 24.00 μL, 0.0226 mmol, 10 mol %) in dry toluene (1 mL). Colorless oil (0.044 g, 54%). R_f (EtOAc/hexane 3:7) = 0.44. $[\alpha]_D^{22}$ = +35.2 (c 2.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 1.01 (d, 3H, J = 7.0 Hz, CH_3), 1.84 (d, 1H, J = 4.0 Hz, O*H*), 2.42 (s, 3H, CH_3), 3.88−3.91 (m, 1H, C*H*), 4.03 (br s, 1H, C*H*), 4.27 (d, 1H, J = 15.5 Hz, C*H*Ph), 4.60 (d, 1H, J = 16.0 Hz, C*H*Ph), 4.78−4.80 (m, 2H, CH_2=

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C═), 5.15 (q, 1H, J = 6.5, 6.5 Hz, CH═C═), 7.23−7.31 (m, 5H, 5CH_{Ar}), 7.37 (d, 2H, J = 7.5 Hz, 2CH_{Ar}), 7.69 (d, 2H, J = 8.5 Hz, 2CH_{Ar}). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 12.4, 21.5, 48.5, 58.6, 71.8, 78.3, 93.0, 127.1, 127.5, 128.2, 128.5, 129.7, 137.7, 137.9, 143.3, 207.0. IR (ν_{max}/cm^{-1}) 3502 (m), 2984 (w), 2922 (w), 1954 (m), 1598 (m), 1333 (s), 1150 (s), 1088 (s), 1002 (s), 863 (S), 732 (s), 657 (s). HRMS (ESI-TOF) m/z calcd for $C_{20}H_{23}NO_3NaS$ $[M + Na]^+$ 380.1296, found 380.1285.

(2*S*,3*R*)-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 (Et_2O/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 Et_2Zn (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 (Et_2O/hexane 1:9) = 0.25. $[\alpha]_D^{22}$ = −36.2 (c 4.1, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 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, 10CH_{Ar}). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 9.2, 54.9, 57.7, 71.1, 76.8, 93.6, 127.2, 128.5, 129.0, 139.9, 207.6. IR (ν_{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.

(4*S*,5*R*)-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 NH_4Cl solution (5 mL), washed with water (10 mL), and dried ($MgSO_4$). 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, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 1.14 (d, 3H, J = 6.6 Hz, CH_3), 3.69−3.78 (m, 1h, CH), 4.03 (d, 1H, J = 15.3 Hz, CHPh), 4.82 (d, 1H, J = 15.0 Hz, CHPh), 4.86−4.98 (m, 3H, CH_2═C═ and CH), 5.17−5.24 (m, 1H, CH═C═), 7.25−7.37 (m, 5H, 5CH_{Ar}). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 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 (ν_{max}/cm^{-1}) 2924 (w), 2358 (w), 1358 (w), 1743 (s), 1675 (m), 1414 (s), 1243 (m), 1159 (m), 761 (m), 700 (s). HRMS (ESI-TOF) m/z calcd for $C_{14}H_{15}NO_2Na$ $[M + Na]^+$ 252.1000, found 252.1003.

(*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 $AuPPh_3NTf_2$ (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 (Et_2O/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 (Et_2O/hexane 7:3) = 0.15. The enantioselectivity was determined by chiral HPLC of the corresponding alcohol using a Phenomenex Lux Cellulose-3 column; hexane/isopropyl alcohol (98:2); flow rate = 0.5 mL/min; 210 nm; t_{major} = 9.83 min, t_{minor} = 10.95 min, 91% ee. $[\alpha]_D^{22}$ = +104.5 (c 0.9, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 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, 5CH_{Ar}). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 15.6, 51.4, 55.5, 75.7, 89.4, 126.8, 127.0, 127.7, 128.0, 128.3, 140.7. IR (ν_{max}/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 $C_{13}H_{18}NO$ $[M + H]^+$ 204.1388, found 204.1393.

(*S*)-*N*-Benzyl-1-((*R*)-2,5-dihydrofuran-2-yl)butan-1-amine (25b). The allenyl precursor was prepared following the general procedure B 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 Et_2Zn (1 M 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 $AuPPh_3NTf_2$ (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 (Et_2O/hexane 2:8). The isolated yield was calculated for the three steps starting from the aldehyde **6b**. Colorless oil (0.26 g, 68%), R_f (Et_2O/hexane 2:8) = 0.30. ^1H NMR (300 MHz, $CDCl_3$) (mixture of two diastereomers, relative integrations given for each diastereomer): δ 0.88 (t, 3H, J = 6.30, 6.9 Hz, CH_3, for each isomer), 1.28−1.49 (br m, 2H, CH_2, 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, CH_2Ph, minor isomer), 3.83 (s, 2H, CH_2Ph, major isomer), 4.58−4.70 (m, 2H, CH_2, 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), 5.90−5.96 (m, 1H, CH═, for each isomer), 7.18−7.30 (m, 5H, 5CH_{Ar}, for each isomer). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) (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 (ν_{max}/cm^{-1}) 3735 (w), 2956 (m), 2871 (m), 2844 (m), 1457 (m), 1354 (w), 1073 (s), 734 (s), 696 (s). HRMS (ESI-TOF) m/z calcd for $C_{15}H_{21}NONa$ $[M + Na]^+$ 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 the general procedure B 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 Et_2Zn (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 $AuPPh_3NTf_2$ (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 (Et_2O/hexane 2:8). The isolated yield was calculated for the three steps starting from the aldehyde **6c**. Colorless oil (0.097 g, 62%), R_f (Et_2O/hexane 2:8) = 0.36. ^1H NMR (300 MHz, $CDCl_3$) (mixture of two diastereomers, relative integrations given for each diastereomer): δ 0.81−0.92 (m, 6H, 2CH_3, 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, CH_2Ph, for each isomer), 4.65−4.69 (m, 2H, CH_2O, 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, 5CH_{Ar}, for each isomer). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) (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 (ν_{max}/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 calcd for $C_{16}H_{24}NO$ $[M + H]^+$ 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 Et_2Zn (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 $AuPPh_3NTf_2$ (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 (Et_2O/hexane 2:8). The isolated yield was

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calculated for the three steps starting from the aldehyde **6d**. Colorless oil (0.263 g, 61%). R_f (Et_2O/hexane 2:8) = 0.22. $[\alpha]_D^{22}$ = −43.3 (*c* 0.65, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 0.98 (d, 6H, *J* = 6.5 Hz, $2CH_3$), 1.84−1.87 (br m, 2H, C*H*, N*H*), 2.37 (br d, 1H, *J* = 3.0 Hz, C*H*), 3.83 (dd, 2H, *J* = 13.0, 12.5 Hz, CH_2Ph), 4.64 (br d, 2H, *J* = 13.0 Hz, CH_2), 4.95 (br s, 1H, C*H*), 5.80 (br s, 1H, C*H*═), 5.93 (br s, 1H, C*H*═), 7.22−7.32 (m, 5H, $5CH_{Ar}$). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 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 (ν_{max}/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 $C_{15}H_{22}NO$ $[M + H]^+$ 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 Et_2Zn (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 $AuPPh_3NTf_2$ (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_f (EtOAc/hexane 3:7) = 0.34. ^1H NMR (500 MHz, $CDCl_3$) (mixture of two diastereomers, relative integrations given for each diastereomer): δ 2.70−2.74 (m, 1H, C*H*Ph, for each isomer), 2.80−2.83 (m, 1H, C*H*Ph, for each isomer), 2.90 (s, 1H, C*H*, minor isomer), 2.98 (br s, 1H, C*H*, major isomer), 3.77 (q, 2H, *J* = 13.5 Hz, CH_2Ph, for each isomer), 4.63−4.73 (m, 2H, 2C*H*−O, for each isomer), 4.89 (br s, 1H, C*H*, for each isomer), 5.78 (br s, 1H, C*H*═, minor isomer), 5.89 (br s, 1H, C*H*═, major isomer), 5.98 (br s, 1H, C*H*═, for each isomer), 7.12−7.27 (m, 10H, $10CH_{Ar}$, for each isomer). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) (mixture of two diastereomers, minor indicated by 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 (ν_{max}/cm^{-1}) 3333 (w), 3026 (w), 2844 (m), 1494 (m), 1452 (m), 1070 (s), 739 (s), 696 (s). HRMS (ESI-TOF) *m*/*z* calcd for $C_{19}H_{22}NO$ $[M + H]^+$ 280.1695, found 280.1697.

***tert*-Butyl 3-((*S*)-2-(Benzylamino)-2-((*R*)-2,5-dihydrofuran-2-yl)ethyl)-1*H*-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)-1*H*-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_2Zn (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 $AuPPh_3NTf_2$ (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, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 1.66 (br s, 9H, $C(CH_3)_3$), 2.76−2.92 (m, 2H, CH_2), 3.07−3.13 (m, 1H, C*H*), 3.81 (dd, 2H, *J* = 13.2, 13.5 Hz, CH_2Ph), 4.63−4.78 (m, 2H, CH_2), 4.95 (br s, 1H, C*H*), 5.93 (br dd, 1H, *J* = 1.2, 0.9 Hz, C*H*), 6.01 (d, 1H, *J* = 6.3 Hz, C*H*), 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}). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 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 (ν_{max}/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 $C_{26}H_{31}N_2O_3$ $[M + H]^+$ 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_2Zn (1 M in toluene, 156.3 μL, 0.145 mmol, 10 mol %) in dry toluene (3 mL). Following the general procedure B, the crude allenyl product was treated with $AuPPh_3NTf_2$ (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_2O/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_2O/hexane 3:7) = 0.18. ^1H 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, C*H*, major isomer), 3.90 (s, 1H, C*H*, minor isomer), 4.47−4.54 (m, 2H, CH_2, for each isomer), 4.97 (br s, 1H C*H*, for each isomer), 5.79−5.81 (m, 1H, C*H*═, for each isomer), 6.02 (br s, 1H, C*H*═, for each isomer). $^{13}C\{^1H\}$ 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 (ν_{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 $C_{13}H_{21}NO_3Na$ $[M + Na]^+$ 262.1419, found 262.1427.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00969.

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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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Wisniewska, H. M.; Jarvo, E. R. *J. Org. Chem.* **2013**, *78*, 11629. (b) Thaima, T.; Zamani, F.; Hyland, C. J. T.; Pyne, S. G. *Synthesis* **2017**, *49*, 1461. (c) Marshall, J. *J. Org. Chem.* **2007**, *72*, 8153. For a review on related allenic stannanes, see: (d) Marshall, J. *Chem. Rev.* **1996**, *96*, 31. (e) Yu, S.; Ma, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 3074. (f) Ma, S. *Chem. Rev.* **2005**, *105*, 2829.

(2) For selected reviews, see: (a) Munoz, M. P. *Chem. Soc. Rev.* **2014**, *43*, 3164. (b) Krause, N.; Winter, C. *Chem. Rev.* **2011**, *111*, 1994.

(3) Hoffmann-Roder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196.

(4) (a) Fandrick, D. R.; Saha, J.; Fandrick, K. R.; Sanyal, S.; Ogikubo, J.; Lee, H.; Roschangar, F.; Song, J. J.; Senanayake, C. H. *Org. Lett.*

DOI: 10.1021/acs.joc.7b00969
J. Org. Chem. 2017, 82, 6819−6830

2011, *13*, 5616. (b) Fandrick, D. R.; Fandrick, K. R.; Reeves, J. T.; Tan, Z.; Johnson, C. S.; Lee, H.; Song, J. J.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2010**, *12*, 88.
(5) Yamashita, Y.; Cui, Y.; Xie, P.; Kobayashi, S. *Org. Lett.* **2015**, *17*, 6042.
(6) (a) Thaima, T.; Pyne, S. G. *Org. Lett.* **2015**, *17*, 778. (b) Liepouri, F.; Bernasconi, G.; Petasis, N. A. *Org. Lett.* **2015**, *17*, 1628. (c) Mangeney, P.; Gérard, H.; Vrancken, E. *Synthesis* **2017**, *49*, 526.
(7) (a) Alcaide, B.; Almendros, P.; del Campo, T. M.; Soriano, E.; Marco-Contelles, J. L. *Chem. - Eur. J.* **2009**, *15*, 9127. (b) Pragani, R.; Roush, W. R. *Org. Lett.* **2008**, *10*, 4613.
(8) (a) Gryko, D.; Chalko, J.; Jurczak, J. *Chirality* **2003**, *15*, 514. For a general review on the reactions of amino aldehydes, see: (b) Reetz, M. T. *Chem. Rev.* **1999**, *99*, 1121.
(9) (a) Ghosh, A. K.; Bischoff, A.; Cappiello, J. *Eur. J. Org. Chem.* **2003**, *2003*, 821. (b) Andrés, J. M.; Pedrosa, R.; Pérez-Encabo, A.; Ramírez, M. *Tetrahedron* **2006**, *62*, 7783.
(10) For selected reviews on oxazolidinone synthesis and bioactivity, see: (a) Diekema, D. J.; Jones, R. N. *Drugs* **2000**, *59*, 7. (b) Michalska, K.; Karpiuk, I.; Król, M.; Tyski, S. *Bioorg. Med. Chem.* **2013**, *21*, 577. (c) Heravi, M. M.; Zadsirjan, V. *Tetrahedron: Asymmetry* **2013**, *24*, 1149.
(11) For a key review on dihydrofuran synthesis and bioactivity, see: (a) Kilroy, T. G.; O'Sullivan, T. P.; Guiry, P. J. *Eur. J. Org. Chem.* **2005**, *2005*, 4929. For selected recent synthetic approaches to 2,5-dihydrofurans, see: (b) Kim, S.; Lee, P. H. *Adv. Synth. Catal.* **2008**, *350*, 547. (c) Shi, T.; Guo, X.; Teng, S.; Hu, W. *Chem. Commun.* **2015**, *51*, 15204. (d) Castarlenas, R.; Vovard, C.; Fischmeister, C.; Dixneuf, P. H. *J. Am. Chem. Soc.* **2006**, *128*, 4079.
(12) (a) Osberger, T. J.; White, M. C. *J. Am. Chem. Soc.* **2014**, *136*, 11176. (b) Fontana, F.; Chen, C. C.; Aggarwal, V. K. *Org. Lett.* **2011**, *13*, 3454.
(13) (a) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12. (b) Le Bras, J.; Muzart, J. *Chem. Soc. Rev.* **2014**, *43*, 3003.
(14) For examples of reactions where *N*-diprotected α-amino aldehydes undergo a switch in diastereoselectivity, see: (a) Jung, C.-K.; Krische, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 17051. (b) Roiban, G.-D.; Ilie, A.; Reetz, M. T. *Chem. Lett.* **2014**, *43*, 2. (c) Hili, R.; Baktharaman, S.; Yudin, A. K. *Eur. J. Org. Chem.* **2008**, *2008*, 5201. (d) Haghshenas, P.; Quail, J. W.; Gravel, M. *J. Org. Chem.* **2016**, *81*, 12075. (e) Haghshenas, P.; Gravel, M. *Org. Lett.* **2016**, *18*, 4518. (f) Martins, B. S.; Moro, A. V.; Lüdtke, D. S. *J. Org. Chem.* **2017**, *82*, 3334.
(15) (a) Heravi, M. M.; Zadsirjan, V. *Tetrahedron: Asymmetry* **2013**, *24*, 1149. (b) Pandit, N.; Singla, R. K.; Shrivastava, B. *Int. J. Med. Chem.* **2012**, *2012*, 159285.
(16) Examination of the ^{1}H NMR spectra at elevated temperature to coalesce rotamer peaks was unsuccessful.
(17) (a) Hashmi, A. S. K.; Blanco, M. C.; Fischer, D.; Bats, J. W. *Eur. J. Org. Chem.* **2006**, *2006*, 1387. (b) Asikainen, M.; Krause, N. *Adv. Synth. Catal.* **2009**, *351*, 2305. (c) Eom, D.; Kang, D.; Lee, P. H. *J. Org. Chem.* **2010**, *75*, 7447. (d) Alcaide, B.; Almendros, P.; del Campo, T. M.; Fernández, I. *Chem. Commun.* **2011**, *47*, 9054. (e) Alcaide, B.; Almendros, P.; Aragoncillo, C.; Gómez-Campillos, G.; Quirós, M. T.; Soriano, E. *J. Org. Chem.* **2016**, *81*, 7362. (f) Hashmi, A. S. K.; Schwarz, L.; Choi, J. H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285. (g) Zhou, C.-Y.; Chan, P. W. H.; Che, C.-M. *Org. Lett.* **2006**, *8*, 325−328.
(18) Dieter, R. K.; Chen, N.; Gore, V. K. *J. Org. Chem.* **2006**, *71*, 8755.
(19) (a) Aurrecoechea, J. M.; Suero, R. *Tetrahedron Lett.* **2005**, *46*, 4945. (b) Aurrecoechea, J. M.; Suero, R.; de Torres, E. *J. Org. Chem.* **2006**, *71*, 8767.
(20) Takacs, J. M.; Jaber, M. R.; Vellekoop, A. S. *J. Org. Chem.* **1998**, *63*, 2742.
(21) (a) Sinha, M.; Dola; Soni, V. R.; Agarwal, A. P.; Srivastava, K.; Haq, W.; Puri, S. K.; Katti, S. B. *Bioorg. Med. Chem.* **2014**, *22*, 5950. (b) Dondoni, A.; Perrone, D.; Merino, P. *J. Org. Chem.* **1995**, *60*, 8074. (c) Cardillo, G.; Fabbroni, S.; Gentilucci, L.; Perciaccante, R.; Tolomelli, A. *Tetrahedron: Asymmetry* **2004**, *15*, 593. (d) Alfaro, R.; Yuste, F.; Ortiz, B.; Sánchez-Obregón, R.; García Ruano, J. L. *Tetrahedron* **2009**, *65*, 357. (e) Unthank, M. G.; Tavassoli, B.; Aggarwal, V. K. *Org. Lett.* **2008**, *10*, 1501. (f) Ho, P. T.; Ngu, K. *J. Org. Chem.* **1993**, *58*, 2313. (g) Albeck, A.; Persky, R. *J. Org. Chem.* **1994**, *59*, 653.
(22) (a) Li, Y.; Dou, D.; He, G.; Lushington, G. H.; Groutas, W. C. *Bioorg. Med. Chem.* **2009**, *17*, 3536. (b) Kuehne, M. E.; Xu, F. *J. Org. Chem.* **1998**, *63*, 9427.
(23) Sato, N.; Ando, M.; Ishikawa, S.; Jitsuoka, M.; Nagai, K.; Takahashi, H.; Sakuraba, A.; Tsuge, H.; Kitazawa, H.; Iwaasa, H.; Mashiko, S.; Gomori, A.; Moriya, R.; Fujino, N.; Ohe, T.; Ishihara, A.; Kanatani, A.; Fukami, T. *J. Med. Chem.* **2009**, *52*, 3385.
(24) Alexakis, A.; Lensen, N.; Tranchier, J.-P.; Mangeney, P.; Feneau-Dupont, J.; Declercq, J. P. *Synthesis* **1995**, *1995*, 1038.
(25) Nickel, S.; Nickel, P.; Hellmert, M.; Ernst, S.; Jewell, R.; Pearce, C. A.; Jones, G.; Hamza, D.; Kaiser, M. *Bioorg. Med. Chem.* **2015**, *23*, 2636.
(26) Garner, P.; Kaniskan, H. U. *Tetrahedron Lett.* **2005**, *46*, 5181.
(27) Cook, G. R.; Stille, J. R. *Tetrahedron* **1994**, *50*, 4105.
(28) Arndt, H. D.; Welz, R.; Muller, S.; Ziemer, B.; Koert, U. *Chem. - Eur. J.* **2004**, *10*, 3945.
(29) Berger, G.; Gelbcke, M.; Cauët, E.; Luhmer, M.; Nève, J.; Dufrasne, F. *Tetrahedron Lett.* **2013**, *54*, 545.
(30) (a) Ghorai, M. K.; Ghosh, K.; Yadav, A. K.; Nanaji, Y.; Halder, S.; Sayyad, M. *J. Org. Chem.* **2013**, *78*, 2311. (b) Golebiowski, A.; Jacobsson, U.; Raczko, J.; Jurczak, J. *J. Org. Chem.* **1989**, *54*, 3759.
(31) (a) Salvatore, R. N.; Nagle, A. S.; Jung, K. W. *J. Org. Chem.* **2002**, *67*, 674. (b) Seo, W. D.; Curtis-Long, M. J.; Ryu, Y. B.; Lee, J. H.; Yang, M. S.; Lee, W. S.; Park, K. H. *J. Org. Chem.* **2006**, *71*, 5008.
(32) Bishop, R. *Org. Synth.* **1992**, *70*, 120.
(33) Jeong, Y.-C.; Moloney, M. *Synlett* **2009**, *2009*, 2487.
(34) Manna, S. K.; Panda, G. *Org. Biomol. Chem.* **2014**, *12*, 8318.
(35) Dondoni, A.; Perrone, D. *Synthesis* **1993**, *1993*, 1162.

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