Development of a Modified System to Provide Improved Diastereocontrol in the Linear-Selective Cu-Catalyzed Reductive Coupling of Ketones and Allenamides

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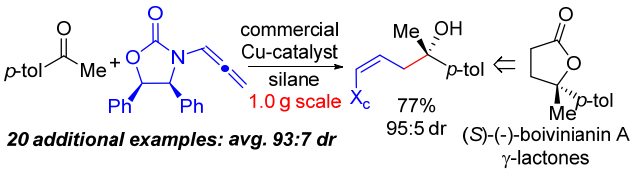
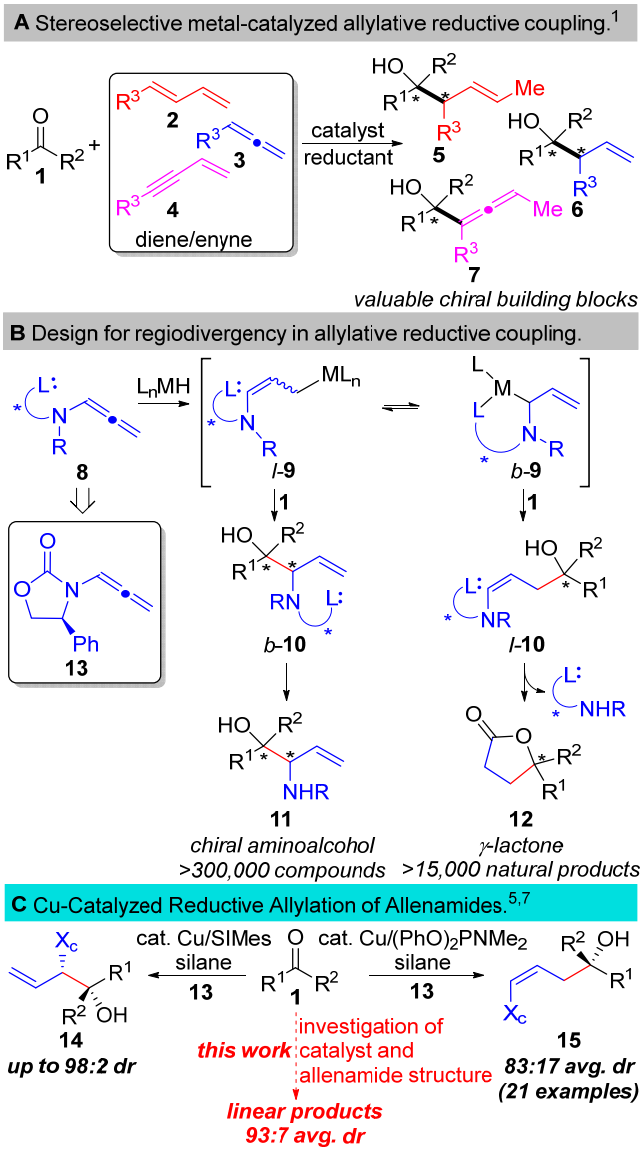
Abstract: Chiral γ-lactones are prevalent organic architectures found in a large array of natural products. In this work, we disclose the development of a modified catalytic system utilizing a commercially available Cu-phosphite catalyst for the diastereoselective reductive coupling of chiral allenamides and ketones to afford chiral γ-lactone precursors in 80:20 to 99:1 dr.



Reductive allylative coupling[1] of carbonyl electrophiles (**1**) and conjugated unsaturated hydrocarbons (*e.g.* **2** – **4**) has emerged as a powerful alternative to classical carbonyl allylation[2] reactions of allylic organometallic reagents (Scheme 1A). These techniques proceed through *in situ* generation of the reactive allyl-organometallic reagent by hydrometalation of the unsaturated hydrocarbon **2** – **4** by a L_nM-H catalyst.[1] Benefits to this approach include: simple reaction setup, enhanced functional group compatibility, and reaction stereocontrol through use of a chiral catalyst. The Krische group[1] has pioneered this new allylation approach employing Ru-, Rh-, or Ir-catalysis using H_2 or autotransfer of H_2 from reactant alcohols to hydrocarbons **2** – **4** to turnover the catalyst.[3] This work typically utilizes primary alcohols or aldehydes as coupling partners. Cu-

catalyzed orthogonal approaches have recently been developed by the Buchwald group[4] utilizing silanes as reductant and ketone or more recently aldehyde electrophiles.

Scheme 1. Reductive Coupling Strategy for Regiodivergent Access to Chiral 1,2-Aminoalcohols and γ-Lactones.



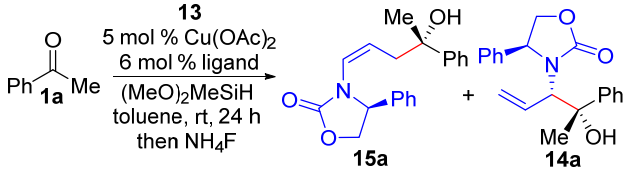
One limitation to these powerful transformations is that branched products (**5** – **7**) are generally formed preferentially to the regioisomeric linear products. General linear-selective processes are rare.[5,6] To address this challenge, our group[5,7] proposed a design strategy based off of directing-group tethered *N*-heteroatom-substituted 1,2-dienes **8** in metal-catalyzed reductive

coupling reactions in an effort to bias the reactivity of the intermediate M(allyl) complexes (**9**) to generate either the branched product *b*-**10** or the linear product *l*-**10** by tuning the ligand on the metal catalyst (Scheme 1B). For instance, selective generation of the linear product (*l*-**10**) may be achieved through preferential formation of *b*-**9** by coordination of the L-group to the catalyst at low metal-coordination numbers. In contrast, inhibition of L-binding (*e.g.* with large or chelating ligands) may prefer branched product *b*-**10**. In either instance, valuable chiral products are accessed in a straightforward manner from simple starting materials. Linear products *l*-**10** may be converted to chiral γ-lactones **12** that are found in >15,000 natural products[8] Alternatively, cleavage of the tether from *b*-**10** allows access to chiral 1,2-aminoalcohols (**11**) that are found in > 300,000 compounds.[9] To validate this concept, chiral allenamide **13** was initially investigated in reductive coupling reactions utilizing ketone electrophiles[5,7a] under Cu-catalysis (Scheme 1C) due to their widespread availability and low cost.[10] Indeed, regiodivergent access to branched (**14**)[7a] or linear **(15)**[5] products could be obtained through use of either a bulky electron-rich *N*-heterocyclic carbene ligand (*e.g.* SIMes or IMes) or a monodentate phosphoramidite ligand, respectively. Importantly, branched products **14** were highly crystalline and could be easily recrystallized to single diastereomers. However, the linear products (**15**) were non-crystalline, and the stereoisomers were typically not separable by chromatography. Furthermore, the diastereoselectivities in the linear-selective process were moderate having an average value of 83:17 dr for the twenty-one examples with a maximum of 97:3 dr. In an effort to improve diastereoselectivities in the linear-selective reductive coupling reaction of allenamides and ketones, detailed investigation into the effect of ligand and allenamide structure on stereocontrol were carried out. The results of these studies are disclosed herein leading to the identification of a

commercially available and cost-effective catalyst system providing high linear regioselection with improved diasterecontrol (average dr of 93:7).

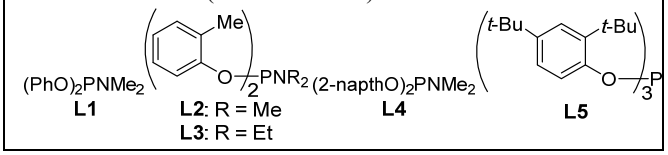
Our previous initial investigations into the ligand employed in the Cu-catalyzed reductive coupling reaction identified that the electron-donating ability[11] of the ligand employed had a significant impact on regiocontrol.[5,7a] For example, as the electron-donating ability of the phosphine ligand decreased upon changing from $P(NMe_3)_3$ to $(PhO)_2PNMe_2$ to $P(OPh)_3$, linear selectivity improved dramatically (Table 2, entries 1, 5, and 10). Initially, **L1** was identified as the optimal ligand for linear-selective reaction (Table 1, entry 5);[5] however, we sought to improve the diastereocontrol above 9:1. Therefore, in the current study, ligands having increased steric effects (*i.e.* larger cone angles)[11a] were later examined (entries 3, 4 and 6 – 9), but the d.r. could not be increased above 92:8.

Table 1. Ligand Investigation Employing Allenamide 13.[a]



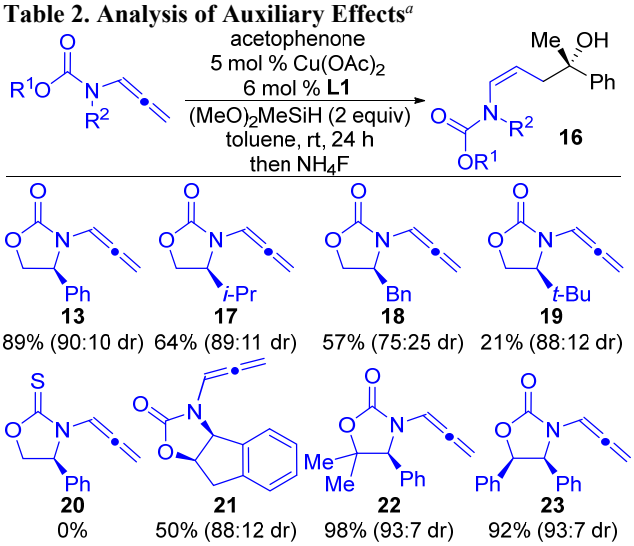
Entry	Ligand	TEP[c]	θ[d]	% **15a** (dr)[e]	*l*:*b*[e]
1[b]	$P(NMe_2)_3$	2062	157	79 (87:13)	83:17
2[b]	$P(OEt)_3$	2076	109	90 (83:17)	92:8
3	$P(O\textit{i}Pr)_3$	2076	130	56 (84:16)	94:6
4	$P(O\textit{t}Bu)_3$	--	172	14 (86:14)	82:18
5[b]	**L1**	--	--	97 (90:10)	97:3
6	**L2**	--	--	42[f] (91:9)	97:3
7	**L3**	--	--	51[f] (92:8)	97:3
8	**L4**	--	--	69 (89:11)	99:1
9[b]	**L5**	2086[g]	175[g]	89 (92:8)	97:3
10[b]	$P(OPh)_3$	2085	128	76 (89:11)	99:1

[a]**1a** (0.25 mmol) and **13** (0.30 mmol) in 0.5 mL of toluene. [b]Data from ref. 5. [c]Tolman electronic parameter from ref 11. [d]Ligand cone angle obtained from ref 18a. [e]Determined by ^{1}HNMR spectroscopy on the unpurified reaction mixture. [f]% conv. [g]Value for $P(O\text{-}o\text{-}C_6H_4\text{-}t\text{-}Bu)_3$ from ref. 11.



Having identified ligand families providing high linear control (*i.e.* phosphoramidites or aryl phosphites), we next investigated the effect of the oxazolidinone motif of the allenamide on stereoselectivity (Table 2) to further improve dr. Replacement of the Ph-group of **13** by other substituents of variable size (*i.e.* **17** – **19**) did not lead to improvements in diastereoselection. Use of the *S*-based derivative (**20**), or that derived from aminoindanol (**21**), were also inferior. Finally, addition of substitution at the oxygen-bearing carbon atom of the oxazolidinone as in SuperQuat auxiliary[12] compound **22** or allenamide **23** allowed for a small increase in diastereoselectivity (93:7 dr).

Table 2. Analysis of Auxiliary Effects[a]

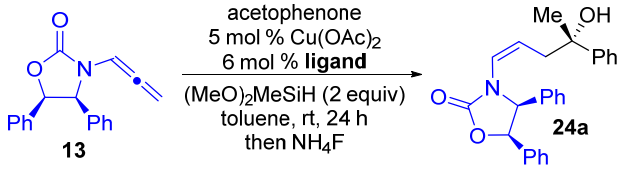


[a]Conditions: Acetophenone (0.250 mmol), allenamide (0.300 mmol), $Cu(OAc)_2$ (5 mol %), **L1** (6 mol %), $Me(MeO)_2SiH$ (0.500 mmol), and 0.50 mL of toluene, rt 24 h followed by treatment with NH_4F/MeOH. Yields represent isolated yield of **16** obtained from the allenamide (**13**, **17-23**) shown.

Based on the results in Tables 1 and 2, a maximum diastereoselectivity of up to 93:7 was obtained either with ligands having large cone angles (Table 1, entries 7 and 9) or through additional carbon-substitution on the oxazolidinone (*e.g.* **22**, **23**, Table 2). To further improve stereoselectivity, we hoped that by combining these two observations, these effects would be

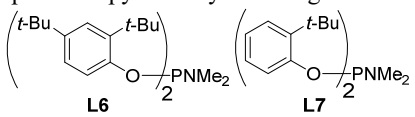
additive. As a result, allenamide **23** was chosen for further development using large cone angle ligands since the aminoalcohol needed to make the oxazolidinone of **23** is commercially available[13] (Table 3). Furthermore, **23** was found to be a stable[14] crystalline solid that was synthesized directly from the oxazolidinone without chromatography in 52% overall yield. Gratifyingly, use of the readily available phosphite ligand **L5**[15] in the reaction of acetophenone with **23** afforded **24a** in moderate yield with excellent diastereoselectivity (96:4 dr, Table 3, entry 1). Our observations from the ligand studies described in Table 1 and previous work[5] indicated that reaction rates decreased as the phosphine became less electron-donating. For instance, reduced yields were obtained with aryl phosphite ligands (Table 1, entry 10) due to incomplete conversion. Similarly, reaction of **23** employing phosphite ligand **L5** had unreacted ketone and allenamide present after 24 h. Doubling the catalyst loading enabled high yield with identical stereocontrol (entry 2). In an effort to improve reactivity, phosphoramidites **L6** and **L7** were prepared and tested (entries 3 and 4). High yields were obtained in these systems using 5 mol % Cu, however, stereoselectivity was reduced. Overall, because both the Cu-precatalyst[16] and **L5** are inexpensive and readily available on large scale, the conditions identified in entry 2 were chosen as optimal since use of 10 mol % catalyst is not cost-prohibitive.

Table 3. Ligand Optimization Employing Allenamide 23.[a]



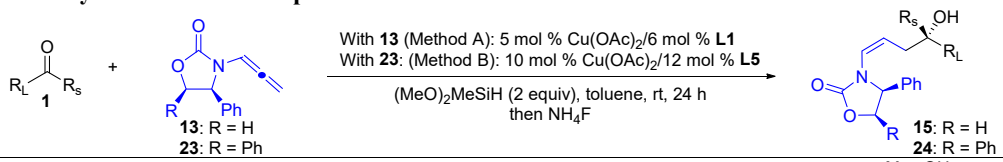
Entry	Ligand	% yield	d.r.
1	**L5**	41	96:4
2[b]	**L5**	92	96:4
3	**L6**	98	93:7
4	**L7**	95	93:7

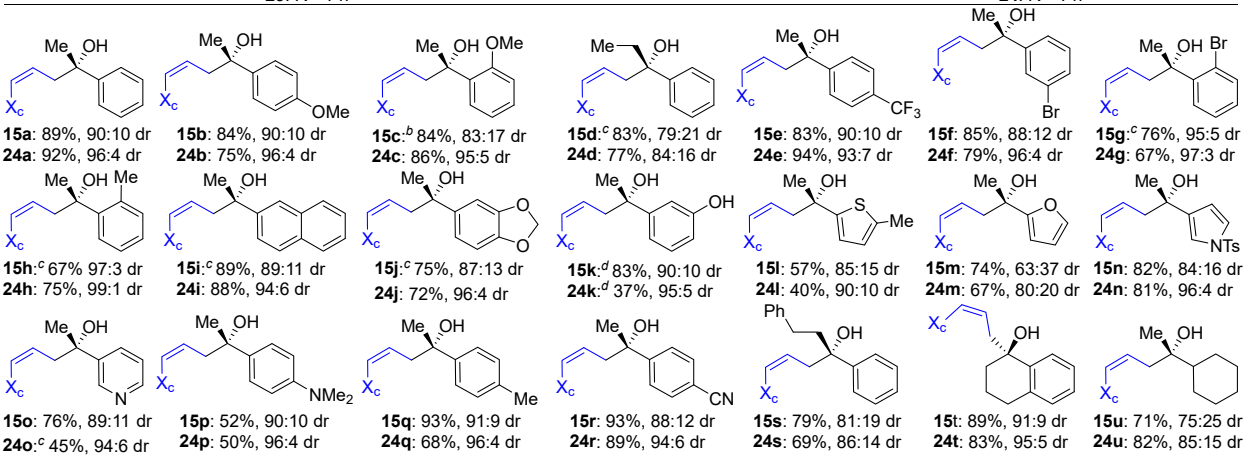
[a]Conditions: acetophenone (0.25 mmol), **13** (0.30 mmol), $Cu(OAc)_2$ (5 mol %), ligand (6 mol %), $Me(MeO)_2SiH$ (0.50 mmol), and 0.5 mL of toluene, rt 24 h followed by treatment with NH_4F/MeOH. *L:b* ratio $\geq$ 97:3 by ^{1}HNMR spectroscopy. [b]Catalyst loading doubled.



After having optimized conditions for improved diastereoselectivity in the linear selective reductive coupling of ketones and allenamides (Table 3, entry 2),[17] the scope of this process was compared to our previous results employing phosphoramidite **L1** and allenamide **13** (Scheme 2).[5] In all cases, the diastereoselectivity was improved by switching to Method B employing phosphite **L5** in conjuction with **23**. Electron-rich (**24b,c,j,p**) or electron-poor (**24e,r**) ketones could be employed with good results along with small 5-membered ring heterocycles (**24l,m,n**). Notably, *ortho*-substitution (**24c,g,h**) was well tolerated providing excellent diastereoselectivities and a reductively-sensitive cyano-group (**24r**) was not reduced under the conditions.

Scheme 2. Analysis of Reaction Scope.[a]



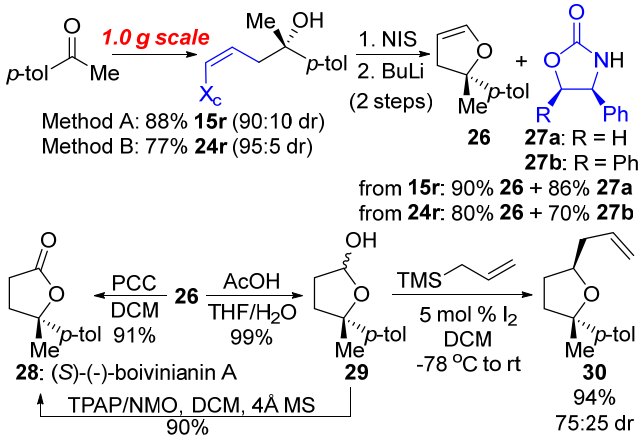


15a: 89%, 90:10 dr; **24a**: 92%, 96:4 dr
15b: 84%, 90:10 dr; **24b**: 75%, 96:4 dr
15c:[b] 84%, 83:17 dr; **24c**: 86%, 95:5 dr
15d:[c] 83%, 79:21 dr; **24d**: 77%, 84:16 dr
15e: 83%, 90:10 dr; **24e**: 94%, 93:7 dr
15f: 85%, 88:12 dr; **24f**: 79%, 96:4 dr
15g:[c] 76%, 95:5 dr; **24g**: 67%, 97:3 dr
15h:[c] 67% 97:3 dr; **24h**: 75%, 99:1 dr
15i:[c] 89%, 89:11 dr; **24i**: 88%, 94:6 dr
15j:[c] 75%, 87:13 dr; **24j**: 72%, 96:4 dr
15k:[d] 83%, 90:10 dr; **24k**:[d] 37%, 95:5 dr
15l: 57%, 85:15 dr; **24l**: 40%, 90:10 dr
15m: 74%, 63:37 dr; **24m**: 67%, 80:20 dr
15n: 82%, 84:16 dr; **24n**: 81%, 96:4 dr
15o: 76%, 89:11 dr; **24o**:[c] 45%, 94:6 dr
15p: 52%, 90:10 dr; **24p**: 50%, 96:4 dr
15q: 93%, 91:9 dr; **24q**: 68%, 96:4 dr
15r: 93%, 88:12 dr; **24r**: 89%, 94:6 dr
15s: 79%, 81:19 dr; **24s**: 69%, 86:14 dr
15t: 89%, 91:9 dr; **24t**: 83%, 95:5 dr
15u: 71%, 75:25 dr; **24u**: 82%, 85:15 dr

[a]See the experimental. Yields are of isolated material and dr's are determined on the unpurified reaction mixture by ^{1}H NMR spectroscopy. *l:b* ratio ≥ 97:3 (^{1}H NMR). [b]Performed at 40 °C. [c]Performed at 60 °C. [d]4.0 equiv of $Me(MeO)_2SiH$ used.

The synthetic utility of the linear-selective Cu-catalyzed reductive coupling of ketones and allenamides is illustrated in Scheme 3. The reaction was readily scaled to 1.0 g on the benchtop using standard Schlenk techniques to provide **15q** or **24q**. Auxiliary removal by enamide hydrolysis could not be carried out using typical acidic conditions due to elimination of the benzylic tertiary alcohol of **15q** or **24q**. Therefore, a convenient and high yielding process was developed consisting of iodocyclization with NIS followed by direct Li/halogen exchange/elimination using *n*-BuLi to provide dihydrofuran **26** along with excellent recovery of the chiral oxazolidinone. Chiral dihydrofuran **26** represents a synthetically versatile intermediate due to the vast array of functionalization reactions known for alkenes (*e.g.* Heck[18] coupling, epoxidation,[19] dihydroxylation,[20] *etc.*). Specifically, **26** could be converted directly to γ-lactone **28** using PCC oxidation[21] to provide the natural product (*S*)-boivoinian A. Alternatively, conversion of the vinyl ether to lactol **29** could be achieved in quantitative yield by acidic hydrolysis. Lactol **29** could subsequently be *C*-allylated using I_2-catalysis[22] to provide **30** or oxidized to lactone **28**.

Scheme 3. Synthetic Utility.



In conclusion, a linear-selective Cu-catalyzed reductive coupling of allenamides and ketones providing improved diastereoselectivities was developed through systematic survey of the allenamide auxiliary and the ligand employed. The Cu-catalyst system disclosed is cheap and commercially available and affords useful synthons *en route* to important chiral γ-lactones with high recovery of the auxiliary.

EXPERIMENTAL SECTION

General. ^{1}H NMR spectra were recorded on Bruker 600 MHz spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, h = hextet, hept = heptet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on Bruker 600 MHz (151 MHz) instrument with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: 77.0 ppm). Liquid chromatography was performed using forced flow (flash chromatography) on silica gel purchased from Silicycle. Thin layer chromatography (TLC) was performed on glass-backed 250 μm silica gel F_{254} plates purchased from Silicycle. Visualization was achieved by using UV light, a 10% solution of phosphomolybdic acid in EtOH or potassium permanganate in water followed by heating. HRMS was collected using a Jeol AccuTOF-DART^{TM} mass spectrometer using DART source ionization. All reactions were conducted in oven or flame dried glassware under an inert atmosphere of nitrogen or argon with magnetic stirring unless otherwise noted. Solvents were obtained from VWR as HPLC grade and transferred to septa sealed bottles, degassed by argon sparge, and analysed by Karl-Fischer titration to ensure water content was ≤ 600 ppm.

$Me(MeO)_2SiH$ was purchased from Alfa Aesar and used as received. Allenamides **13**, **17**, and **18** were prepared according to the literature.[10] Ketones were purchased from Sigma Aldrich, Combi-Blocks, TCI America, Alfa Aesar or Oakwood Chemicals and used as received. $Cu(OAc)_2$ was purchased from the Strem Chemical Company and used as received. All other materials were purchased from VWR, Sigma Aldrich, Combi-Blocks, or Alfa Aesar and used as received.

Ligand Syntheses:

Di-*o*-tolyl dimethylphosphoramidite (L2). A solution of 0.928 g (8.58 mmol) of *o*-cresol and 0.70 g (4.3 mmol) of hexamethylphosphorous triamide in 1.6 mL of 1,2-dimethoxyethane was refluxed for 24 h under an argon atmosphere using an oil bath. Volatile material was removed *in vacuo*, and the resultant residue was purified by bulb-to-bulb distillation under vacuum (~2 torr) to provide 1.07 g (86%) of **L2** as a colorless oil. ^{1}HNMR ($CDCl_3$, 600 MHz) δ: 7.16 (d, J = 7.4 Hz, 2H), 7.09 (t, J = 7.0 Hz, 2H), 6.93 – 6.99 (m, 4H), 2.83 (d, $^3J_{P\text{-}H}$ = 9.5 Hz, 6H), 2.22 (s, 6H) ppm. ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 151.9 ($J_{C\text{-}P}$ = 5.5 Hz), 131.0, 129.7 ($J_{C\text{-}P}$ = 2.4 Hz), 126.7, 122.9, 119.4 ($J_{C\text{-}P}$ = 13 Hz), 34.9 ($J_{C\text{-}P}$ = 20 Hz), 16.6 ppm. ^{31}P NMR (242 MHz, $CDCl_3$): 139.8 ppm. HRMS (DART) *m/z* calcd for $C_{16}H_{21}NO_2P$ $[M + H]^+$: 290.1310; Found $[M + H]^+$: 290.1328.

Di-*o*-tolyl diethylphosphoramidite (L3). A solution of 0.787 g (7.28 mmol) of *o*-cresol and 0.90 g (3.6 mmol) of hexaethylphosphorous triamide in 1.4 mL of 1,2-dimethoxyethane was refluxed for 24 h under an argon atmosphere using an oil bath. Volatile material was removed *in vacuo*, and the resultant residue was purified by bulb-to-bulb distillation under vacuum (~2 torr) to provide 0.938 g (81%) of **L3** as a colorless oil. ^{1}HNMR ($CDCl_3$, 600 MHz) δ: 7.15 (d, J = 7.4 Hz, 2H), 7.08 (t, J = 7.9 Hz, 2H), 7.01 (d, J = 7.9 Hz, 2H), 6.94 (t, J = 7.4 Hz, 2H), 3.31 (dq, $^3J_{P\text{-}H}$ = 10 Hz, $^3J_{H\text{-}H}$ = 7.1 Hz, 4H), 2.22 (s, 6H), 1.14 (t, J = 7.1 Hz, 6H) ppm. ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.3 ($J_{C\text{-}P}$ = 6.4 Hz), 131.0, 129.6 ($J_{C\text{-}P}$ = 2.4 Hz), 126.6, 122.7, 119.2 ($J_{C\text{-}P}$ = 14 Hz), 38.0 ($J_{C\text{-}P}$ = 22 Hz), 16.7, 14.8 ($J_{C\text{-}P}$ = 3.3 Hz) ppm. ^{31}P NMR (242 MHz, $CDCl_3$): 140.7 ppm. HRMS (DART) *m/z* calcd for $C_{18}H_{25}NO_2P$ $[M + H]^+$: 318.1623; Found $[M + H]^+$: 318.1637.

Di(naphthalen-2-yl) dimethylphosphoramidite (L4). A solution of 0.53 g (3.7 mmol) of 2-napthol and 0.30 g (1.8 mmol) of hexamethylphosphorous triamide in 1.0 mL of 1,2-dimethoxyethane was refluxed for 2 h under an argon atmosphere using an oil bath. Volatile material was removed *in vacuo* to afford a solid. This solid was triturated with 5 mL of heptane, isolated by filtration, and dried *in vacuo* to afford 0.319 g (48%) of **L4** as a white solid. M.p. 65 – 67 ºC. ^{1}HNMR ($CDCl_3$, 600 MHz) δ: 7.80 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.7 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H), 7.43 – 7.47 (m, 4H), 7.39 (t, J = 7.3 Hz, 2H), 7.28 (dd, J = 8.7, 2.0 Hz, 2H), 2.86 (d, $^3J_{P\text{-}H}$ = 9.4 Hz, 6H) ppm. ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 151.4 ($J_{C\text{-}P}$ = 6.5 Hz), 134.3, 130.0, 129.6, 127.6, 127.0, 126.3, 124.5, 121.2 ($J_{C\text{-}P}$ = 5.9 Hz), 115.3 ($J_{C\text{-}P}$ = 11 Hz), 34.9 ($J_{C\text{-}P}$ = 21 Hz) ppm. ^{31}P NMR (242 MHz, $CDCl_3$): 139.5 ppm. HRMS (DART) *m/z* calcd for $C_{22}H_{21}NO_2P$ $[M + H]^+$: 362.1310; Found $[M + H]^+$: 362.1306.

Bis(2,4-di-*tert*-butylphenyl) dimethylphosphoramidite (L6). A solution of 0.885 g (4.29 mmol) of 2,4-di-*tert*-butylphenol and 0.35 g (2.1 mmol) of hexamethylphosphorous triamide in 1.2 mL of xylenes was refluxed for 48 h under an argon atmosphere using an oil bath. Volatile material was removed *in vacuo*, and the resultant residue was purified by flash chromatography using nitrogen to pressurize the column (gradient, 0 – 5% EtOAc in hexanes) to provide 0.660 g (63%) of **L6** as a thick viscous oil. R_f = 0.75 (5%

EtOAc/hexanes). ^{1}HNMR ($CDCl_3$, 600 MHz) δ: 7.35 (d, J = 1.9 Hz, 2H), 7.09 (dd, J = 8.4, 1.9 Hz, 2H), 6.99 (dd, J = 8.4, 1.9 Hz, 2H), 2.82 (d, $^{3}J_{P-H}$ = 9.2 Hz, 6H), 1.41 (s, 18H), 1.30 (s, 18H) ppm. $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 150.7 (J_{C-P} = 8.3 Hz), 144.0, 138.5 (J_{C-P} = 2.1 Hz), 124.2, 123.3, 117.2 (J_{C-P} = 22 Hz), 35.4 (J_{C-P} = 21 Hz), 35.0, 34.4, 31.6, 30.0 ppm. ^{31}P NMR (242 MHz, $CDCl_3$): 136.6 ppm. HRMS (DART) *m/z* calcd for $C_{30}H_{49}NO_2P$ $[M + H]^+$: 486.3501; Found $[M + H]^+$: 486.3531.

Bis(2-(*tert*-butyl)phenyl) dimethylphosphoramidite (L7). A solution of 0.644 g (4.29 mmol) of 2-*tert*-butylphenol and 0.35 g (2.1 mmol) of hexamethylphosphorous triamide in 1.2 mL of xylenes was refluxed for 24 h under an argon atmosphere using an oil bath. Volatile material was removed by distillation *in vacuo*, and upon cooling to ambient temperature, the crude residue solidified upon standing. The resultant solid was then triturated with 5 mL of 80:20 IPA:H_2O and collected by filtration. The final solid was dried *in vacuo* at 30 ºC overnight to provide 0.501 g (63%) of **L7** as a white solid. M.p. 51 – 53 ºC. ^{1}HNMR ($CDCl_3$, 600 MHz) δ: 7.33 (d, J = 7.7 Hz, 2H), 7.05 – 7.12 (m, 4H), 6.96 (t, J = 6.7 Hz, 2H), 2.84 (d, $^{3}J_{P-H}$ = 9.4 Hz, 6H), 1.41 (s, 18H) ppm. $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 153.1 (J_{C-P} = 8.0 Hz), 139.5 (J_{C-P} = 2.2 Hz), 127.1, 126.8, 121.9, 117.8 (J_{C-P} = 22 Hz), 35.5 (J_{C-P} = 21 Hz), 34.8, 12.9 ppm. ^{31}P NMR (242 MHz, $CDCl_3$): 136.2 ppm. HRMS (DART) *m/z* calcd for $C_{22}H_{33}NO_2P$ $[M + H]^+$: 374.2249; Found $[M + H]^+$: 374.2259.

(*S*)-4-(*tert*-butyl)-3-(propa-1,2-dien-1-yl)oxazolidin-2-one (19). (*S*)-4-*tert*-Butyloxazolidin-2-one (0.1 g, 0.6 mmol)[23] was treated with (0.07 g, 0.63mmol) of ^{t}BuOK in a dried 3-neck flask in 20 ml DMSO for 30 min in room temperature. The temperature was cooled to 17 ºC and kept not higher than 27 ºC while (0.1 g, 0.8 mmol) of propargyl bromide (80 wt% in toluene) was added dropwise. The reaction was stirred for 3 h and monitored by TLC or HPLC. The completed reaction was quenched by 10 ml of water and extracted with MTBE (2x10ml) and then dried by $MgSO_4$ and concentrated *in vacuo*. The product can be used without any further purification. The rearrangement from alkyne to allene via adding portion wise ^{t}BuOK(5x 18.6 mg) in 20 ml THF and was monitored by HPLC or TLC. The complete reaction was quenched by 10 ml of water and extracted with MTBE (2x10ml) and then dried by $MgSO_4$ and concentrated *in vacuo*. The title compound was purified by silica gel chromatography (eluent: 0 – 30% EtOAc in hexanes) to provide desired product as a red oil (0.08 g, 80% yield). R_f = 0.23 (50% EtOAc/hexanes). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 6.86 (t, J = 6.5 Hz, 1H), 5.39 (dd, J = 10, 6.5 Hz, 1H), 5.35 (dd, J = 10, 6.5 Hz, 1H), 4.30 – 4.24 (m, 2H), 3.59 (dd, J = 7.6, 2.7 Hz, 1H), 0.96 (s, 9H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 202.3, 156.6, 98.5, 88.1, 65.6, 62.4, 35.3, 25.9. HRMS (DART) m/z calcd for $C_{10}H_{16}NO_2$ $[M + H]^+$: 182.1181; Found $[M + H]^+$: 182.1209.

(*S*)-4-phenyl-3-(propa-1,2-dien-1-yl)oxazolidine-2-thione (20). (*S*)-2-phenyl-2-(prop-2-yn-1-ylamino)ethan-1-ol (0.5g, 3mmol)[24] was treat with 1,1'-thiocarbonyldiimidazole (0.5g, 3 mmol) in 20 ml CH_2Cl_2 for 6 h.[25] The reaction was quenched by 10ml water, extracted by 2x10ml CH_2Cl_2 then dried by $MgSO_4$ and concentrated *in vacuo*. The *N*-propargyl oxazolidinthione intermediate was purified by silica gel chromatography (eluent: 0 – 30% EtOAc in hexanes) to provide this material as a yellow oil (0.4 g, 60% yield). The rearrangement from alkyne to allene was performed by adding portion wise ^{t}BuOK (3x0.06g) in 30 ml THF and was monitor by HPLC or TLC. The complete reaction was quenched by 10 ml water and extracted by (2x10ml) MBTE

then dried by $MgSO_4$ and concentrated *in vacuo*. The title compound was purified by silica gel chromatography (eluent: 0 – 30% EtOAc in hexanes) to provide desired product as a red oil (0.2 g, 20% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.40 – 7.33 (m, 4H), 7.21 (dd, *J* = 7.8, 1.7 Hz, 2H), 5.25 (dd, *J* = 11, 6.5 Hz, 1H), 5.08 (dd, *J* = 9.1, 5.1 Hz, 1H), 4.96 (dd, *J* = 11, 6.5 Hz, 1H), 4.86 (t, *J* = 9.1 Hz, 1H), 4.40 (dd, *J* = 9.1, 5.1 Hz, 1H).^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 203.0, 185.2, 137.7, 129.2, 129.1, 126.5, 97.8, 87.8, 74.6, 62.7. HRMS (DART) m/z calcd for $C_{12}H_{12}NOS$ $[M + H]^+$: 218.0640; Found $[M + H]^+$: 218.0649.

Aminoindanol-derived allenamide 21. (3a*R*,8a*S*)-3,3a,8,8a-tetrahydro-2H-indeno[1,2-d]oxazol-2-one (0.34 g, 2.31 mmol)[23] were treated with (2.47g, 2.2 mmol) ^{t}BuOK in a dried 3-neck flask in 20 ml DMSO for 30min in room temperature. The temperature was cooled to 17 ºC and kept not higher than 27 ºC while (3.4 g, 2.3 mmmol) of propargyl bromide (80 wt% in toluene) was adding dropwise. The reaction was stirred for 5h and monitored by TLC or HPLC. The completed reaction was quenched by 10ml water and extracted by (2x10ml) MTBE then dried by $MgSO_4$ and concentrated *in vacuo*. The product can be used without any further purification. The rearrangement from alkyne to allene via adding portion wise ^{t}BuOK (3x20mg) in 20 ml THF and was monitor by HPLC or TLC. The complete reaction was quenched by 10 ml water and extracted by (2x10ml) MBTE then dried by $MgSO_4$ and concentrated *in vacuo*. The title compound was purified by silica gel chromatography (eluent: 0 – 30% EtOAc in hexanes) to provide desired product as a red oild (0.35 g, 81% yield). R_f = 0.24 (50% EtOAc/hexanes). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 7.7 Hz, 1H), 7.32 – 7.09 (m, 3H), 6.82 (t, *J* = 6.5 Hz, 1H), 5.62 (dd, *J* = 10, 6.5 Hz, 1H), 5.49 (dd, *J* = 10, 6.5 Hz, 1H), 5.24 – 5.28 (m, 1H), 5.20 (d, *J* = 7.2 Hz, 1H), 3.27 – 3.36 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 201.4, 154.4, 140.2, 138.4, 129.6, 127.7, 126.2, 125.5, 96.6, 88.5, 78.5, 63.3, 38.3. HRMS (DART) m/z calcd for $C_{13}H_{12}NO_2$ $[M + H]^+$: 214.0868; Found $[M + H]^+$: 214.0876.

(*S*)-5,5-dimethyl-4-phenyl-3-(propa-1,2-dien-1-yl)oxazolidin-2-one (22). To a solution of 500.0 mg (2.61 mmol) of (*S*)-5,5-dimethyl-4-phenyloxazolidin-2-one in 5.0 mL of DMSO was charged 308.0 mg (2.75 mmol) of KO^{t}Bu. The resulting solution was then stirred for 30 mins. The solution was cooled to 20 ºC and 0.32 mL (2.88 mmol, 80 wt% in toluene) of propargyl bromide was added slowly whilst ensuring the temperature did not exceed 23 ºC. The solution was then allowed to warm to rt. Whilst monitoring the reaction with HPLC, small portions (30.0 mg) of KO^{t}Bu was added over time until >99:1 allene:alkyne was observed. To the mixture was charged 15 mL of deionized water and extracted with ethyl acetate (3 x10). The combined organics was decolorized with activated charcoal, dried with Na_2SO_4 and concentrated *in vacuo*. The crude residue was then purified by flash chromatography on silica gel (eluent: 10 – 30% EtOAc in hexanes) to afford 278 mg (46%) of the title compound as an off white solid. M.p. 112 – 113 ºC. R_f = 0.25 (25% EtOAc/hexanes). ^{1}HNMR ($CDCl_3$, 600 MHz) δ:7.30 – 7.38 (m, 3H), 7.11 (d, *J* = 6.44 Hz, 2H), 6.87 (t, *J* = 6.7 Hz, 1H), 5.10 (dd, *J* = 10.7 Hz, 6.2 Hz, 1H), 4.79 (dd, *J* = 9.7 Hz, *J* = 6.6 Hz, 1H), 4.49 (s, 1H), 1.60 (s, 3H), 0.95 (s, 3H) ppm. ^{13}C (151 MHz, $CDCl_3$) δ: 202.1, 154.7,

135.3, 128.5, 128.4, 95.9, 87.1, 82.2, 68.5, 29.0, 24.0 ppm. HRMS (DART) *m/z* calcd for C14H15NO2 [M + H]+: 229.1103; Found [M + H]+: 229.1103

(4*S*,5*R*)-4,5-diphenyl-3-(propa-1,2-dien-1-yl)oxazolidine-2-one (23). (4*S*,5*R*)-4,5-diphenyloxazolidin-2-one[26] (6g, 0.02 mol) was treated with (2g, 0.022mol) ^{t}BuOK in a dried 3-neck flask in 40 ml DMSO for 40 min in room temperature. The temperature was cooled to 17ºC and kept not higher than 27 ºC while (3g, 0.022 mol) propargyl bromide (80 wt% in toluene) was added dropwise. The reaction was stirred for 3h and monitored by TLC or HPLC. The completed reaction was quenched by 30ml water and extracted by (3x30ml) MTBE then dried by $MgSO_4$ and concentrated *in vacuo*. The product can be used without any further purification. The rearrangement from alkyne to allene via adding (3x0.1g) ^{t}BuOK in 40ml THF and was monitor by HPLC or TLC. The complete reaction was quenched by 30 ml water and extracted by (3x30ml) MBTE then dried by MgSO4 and concentrated *in vacuo*. The title product was purified by recrystallization in IPA/Water (20:80) to provide desired product as a white solid (3.5 g, 52% yield). Spectral data matched that previously reported.[27]

General Procedure for the Cu-catalyzed reductive coupling of allenamides and ketones. The procedure for Method A, and the characterization data for products **15** are described elsewhere.[5] Method B procedure: To a 20 mL crimp-cap vial with stir-bar in an Ar-filled glove-box was charged 9.1 mg (0.050 mmol) of $Cu(OAc)_2$ and 17.0 mg (0.060 mmol) of **L5**. Toluene (1.0 mL) was then charged, and the mixture was stirred for 15 min. Allenamide **23** (0.17 g, 0.60 mmol) followed by ketone (0.50 mmol) were then charged, and the vial was sealed with a crimp-cap septum and removed from the glove-box. The reaction was then cooled in an ice bath, and dimethoxymethylsilane (0.12 mL, 2 equiv) was charged by syringe. The mixture was then allowed to warm to rt and stirred for 24 h. The reaction was then quenched by the addition of 95 mg of NH_4F and 3.0 mL of MeOH followed by agitation at rt for 30 min – 1 h. To the mixture was then charged 10 mL of 5% $NaHCO_3$ followed by extraction with DCM (2x8mL). The combined organics were dried with Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel to afford the desired product. Stereochemistry is assigned by analogy to compounds **15** determined previously.[5]

(4*S*)-3-(4-hydroxy-4-phenylpent-1-en-1-yl)-4-isopropyloxazolidin-2-one (31). Prepared according to the general procedure using allenamide **17**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 46 mg (50%) of product as a yellow oil as an 89:11 mixture of diasteromers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.25 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.23 (t, *J* = 7.3 Hz, 1H), 5.68 (d, *J* = 8.7 Hz, 1H), 5.04 – 5.12 (m, 1H), 4.32 (t, *J* = 8.9 Hz, 1H), 4.12 (dd, *J* = 8.8, 6.5 Hz, 1H), 4.03 (s, 1H), 3.80 – 3.88 (m, 1H), 2.79 (dd, *J* = 14.6, 9.6 Hz, 1H), 2.58 (dd, *J* = 14.6, 5.9 Hz, 1H), 1.89 – 2.00 (m, 1H), 1.60 (s, 3H), 0.89 (d, *J* = 7.0 Hz, 3H), 0.86 (d, *J* = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.9, 147.5, 128.1, 126.5, 125.0, 123.7, 122.5, 73.1, 63.6, 61.9, 42.0, 31.8, 29.0, 17.5, 14.9. HRMS (DART) m/z calcd for $C_{17}H_{24}NO_3$ [M + H]$^+$: 290.1756; Found [M + H]$^+$: 290.1756.

(4*R*)-4-benzyl-3-(4-hydroxy-4-phenylpent-1-en-1-yl)oxazolidin-2-one (32). Prepared according to the general procedure using allenamide **18**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 48 mg (57%) of product as a white oil as a 75:25 mixture of diasteromers (determined by ^{1}HNMR spectroscopic analysis). Rf = 0.3 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.43 (d, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.14 – 7.25 (m, 4H), 7.03 (d, *J* = 8.0 Hz, 2H), 5.75 (d, *J* = 8.8 Hz, 1H), 5.11 (dt, *J* = 8.8, 6.6 Hz, 1H), 4.16 (q, *J* = 8.3 Hz, 1H), 4.07 – 4.14 (m, 1H), 4.02 (dd, *J* = 8.6, 5.8 Hz, 1H), 3.59 (s, 1H), 2.96 (dd, *J* = 14, 4.1 Hz, 1H), 2.71 (dd, *J* = 14, 9.0 Hz, 1H), 2.55 – 2.62 (m, 2H), 1.55 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.5, 147.5, 135.0, 129.2, 129.0, 128.2, 127.3, 126.6, 125.0, 123.4, 121.9, 73.4, 66.8, 58.3, 42.1, 38.6, 31.4. HRMS (DART) m/z calcd for $C_{21}H_{24}NO_3$ $[M + H]^+$: 338.1756; Found $[M + H]^+$: 338.1778.

(4*S*)-4-(*tert*-butyl)-3-(4-hydroxy-4-phenylpent-1-en-1-yl)oxazolidin-2-one (33). Prepared according to the general procedure using allenamide **19**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 32 mg (21%) of product as a pale yellow oil as a 88:12 mixture of diasteromers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.25 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.51 (d, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 5.59 (d, *J* = 8.3 Hz, 1H), 5.02 – 5.10 (m, 1H), 4.43 (s, 1H), 4.33 (t, *J* = 9.2 Hz, 1H), 4.19 (t, *J* = 7.7 Hz, 1H), 3.55 (t, *J* = 9.0 Hz, 1H), 2.91 (app. t, *J* = 14.5 Hz, 1H), 2.53 – 2.62 (m, 1H), 1.62 (s, 3H), 0.91 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.5, 146.3, 127.0, 125.5, 125.3, 124.1, 122.6, 71.9, 65.6, 63.6, 41.3, 33.3, 31.6, 24.5. HRMS (DART) m/z calcd for $C_{28}H_{26}NO_3$ $[M + H]^+$: 304.1913; Found $[M + H]^+$: 304.1912.

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(3a*R*,8a*R*)-3-(4-hydroxy-4-phenylpent-1-en-1-yl)-3,3a,8,8a-tetrahydro-2*H*-indeno[1,2-*d*]oxazol-2-one (34). Prepared according to the general procedure using allenamide **21**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 84 mg (50%) of product as a yellow oil as an 88:12 mixture of diasteromers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.23 (50% EtOAc/hexanes). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.48 – 7.42 (m, 2H), 7.37 – 7.21 (m, 8H), 6.02 (dt, *J* = 8.6, 1H), 5.39 – 5.30 (m, 1H), 5.27 (d, *J* = 7.5 Hz, 1H), 5.26 – 5.20 (m, 1H), 3.63 (s, 1H), 3.44 (dd, *J* = 18, 6.5 Hz, 1H), 3.38 (d, *J* = 18 Hz, 1H), 2.64 (dd, *J* = 15, 8.9 Hz, 1H), 2.52 (ddd, *J* = 15, 6.7, 1.9 Hz, 1H), 1.54 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 155.9, 147.5, 140.1, 138.6, 129.8, 128.1, 127.7, 126.6, 125.7, 125.1, 124.9, 123.3, 122.5, 77.9, 73.4, 65.7, 41.8, 38.7, 31.2. HRMS (DART) m/z calcd for $C_{21}H_{22}NO_3$ $[M + H]^+$: 336.1600; Found $[M + H]^+$: 336.1611.

(S)-3-((S,Z)-4-hydroxy-4-phenylpent-1-en-1-yl)-5,5-dimethyl-4-phenyloxazolidin-2-one (35). Prepared according to the general procedure using allenamide **22**. The product was purified by silica gel chromatography (eluent: 20 – 50% EtOAc in hexanes) to provide 82.5 mg (93%) of product as a thick glass as an 89:11 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.21 (40% EtOAc/hexanes). ^{1}HNMR ($CDCl_3$, 600 MHz) δ: 7.44 (d,

J = 8.0 Hz, 2H), 7.34-7.39 (m, 3H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.37 (d, *J* = 7.4 Hz, 2H), 5.81 (d, *J* = 9.3 Hz, 1H), 4.98 (q, *J* = 8.0 Hz, 1H), 4.68 (s, 1H), 3.52 (s, 1H), 2.68 (dd, *J* = 15.4 Hz, 9.0 Hz, 1H), 2.61 (dd, *J* = 15.0 Hz, 6.8 Hz, 1H), 1.59 (s, 3H), 1.51 (s, 3H), 0.95 (s, 3H) ppm. ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ: 156.1, 147.7, 135.1, 128.8, 128.7, 128.1, 128.0, 127.0, 126.4, 124.8, 124.7, 124.3, 124.1, 118.6, 82.0, 73.3, 73.2, 70.8, 41.7, 41.5, 30.6, 30.1, 29.6, 28.6, 28.5, 23.8 ppm. HRMS (DART) *m/z* calcd for $C_{22}H_{24}NO_2$ $[M - OH]^+$: 334.1802; Found $[M - OH]^+$: 334.1789.

(4*S*,5*R*)-3-(4-hydroxy-4-phenylpent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24a). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.19 g (92%) of **24a** as a white foam as a 95:5 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.27 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.42 (d, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.7 Hz, 2H), 7.25 (q, *J* = 6.9 Hz, 1H), 7.05 – 7.16 (m, 6H), 6.96 (d, *J* = 4.4 Hz, 2H), 6.81 (d, *J* = 6.9 Hz, 2H), 6.05 (d, *J* = 9.2 Hz, 1H), 5.86 (d, *J* = 8.0 Hz, 1H), 5.23 (d, *J* = 8.0 Hz, 1H), 5.04 (q, *J* = 8.2 Hz, 1H), 3.03 (s, 1H), 2.71 – 2.54 (m, 2H), 1.49 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.7, 147.9, 133.83, 133.80, 128.5, 128.4, 128.25, 128.19, 128.0, 127.4, 126.6, 126.2, 124.8, 123.7, 117.1, 80.2, 73.5, 66.2, 41.5, 29.9. HRMS (DART) m/z calcd for $C_{26}H_{26}NO_3$ $[M + H]^+$: 400.1913; Found $[M + H]^+$: 400.1918.

(4*S*,5*R*)-3-(4-hydroxy-4-(4-methoxyphenyl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24b). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.16 g (75%) of **24b** as a white solid as a 96:4 mixture of diasteromers (determined by ^{1}HNMR spectroscopic analysis). Mp – 140-142 °C. R_f = 0.3 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.33 – 7.30 (m, 2H), 7.15 – 7.07 (m, 6H), 7.02 – 6.92 (m, 2H), 6.87 – 6.83 (m, 2H), 6.81 – 6.77 (m, 2H), 6.05 (dt, *J* = 9.2, 1.6 Hz, 1H), 5.85 (d, *J* = 8.0 Hz, 1H), 5.22 (d, *J* = 8.0 Hz, 1H), 5.01 (q, *J* = 9.2 Hz, 1H), 3.80 (s, 3H), 2.81 (s, 1H), 2.66 – 2.46 (m, 2H), 1.46 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 158.3, 156.7, 140.0, 133.84, 133.78, 128.45, 128.40, 128.2, 128.0, 127.4, 126.2, 126.0, 123.6, 117.0, 113.5, 80.1, 73.3, 66.2, 55.3, 41.6, 29.9. HRMS (DART) m/z calcd for $C_{27}H_{28}NO_4$ $[M + H]^+$: 430.2018; Found $[M + H]^+$: 430.2048.

(4*S*,5*R*)-3-(4-hydroxy-4-(2-methoxyphenyl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24c). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.18 g (86%) of **24c** as a white oil as a 95:5 mixture of diasteromers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.3 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.30 – 7.26 (m, 2H), 7.15 – 7.09 (m, 6H), 7.00 – 6.97 (m, 3H), 6.97 – 6.91 (m, 1H), 6.84 – 6.80 (m, 2H), 6.10 (dt, *J* = 9.2, 1.7 Hz, 1H), 5.86 (d, *J* = 7.9 Hz, 1H), 5.25 (d, *J* = 7.9 Hz, 1H), 5.03 (dt, *J* = 9.2, 7.3 Hz, 1H), 4.25 (s, 1H), 3.87 (s, 3H), 2.84 (ddd, *J* = 15.1, 7.1, 1.9 Hz, 1H), 2.65 (ddd,

J = 15.1, 7.6, 1.7 Hz, 1H), 1.47 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 156.7, 156.6, 134.2, 134.0, 133.9, 128.36, 128.33, 128.2, 127.9, 127.4, 127.0, 126.2, 122.84, 122.76, 120.9, 117.6, 111.2, 80.1, 74.2, 66.2, 55.3, 39.3, 27.1. HRMS (DART) m/z calcd for $C_{27}H_{28}NO_4$ $[M + H]^+$: 430.2018; Found $[M + H]^+$: 430.2003.

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(4*S*,5*R*)-3-(4-hydroxy-4-phenylhex-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24d). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.16 g (77%) of **24d** as a white solid as an 84:16 mixture of diasteromers (determined by ^{1}HNMR spectroscopic analysis). Mp – 140-141 ºC R_f = 0.3 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.39 – 7.35 (m, 2H), 7.35 – 7.29 (m, 2H), 7.25 – 7.19 (m, 1H), 7.15 – 7.02 (m, 6H), 6.97 – 6.93 (m, 2H), 6.81 – 6.77 (m, 2H), 5.95 (dt, *J* = 9.1, 1.5 Hz, 1H), 5.86 (d, *J* = 8.0 Hz, 1H), 5.24 (d, *J* = 8.1 Hz, 1H), 4.99 (dt, *J* = 9.0, 6.5 Hz, 1H), 2.92 (s, 1H), 2.68 (ddd, *J* = 14.8, 9.0, 1.3 Hz, 1H), 2.60 (ddd, *J* = 14.8, 6.5, 1.9 Hz, 1H), 1.80 (q, *J* = 7.5 Hz, 2H), 0.73 (t, *J* = 7.5 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 156.7, 145.8, 133.9, 133.8, 128.44, 128.37, 128.2, 128.1, 128.0, 127.4, 126.4, 126.1, 125.4, 123.8, 118.1, 80.1, 76.0, 66.3, 40.2, 34.5, 7.9. HRMS (DART) m/z calcd for $C_{27}H_{28}NO_3$ $[M + H]^+$: 414.2069; Found $[M + H]^+$: 414.2098.

(4*S*,5*R*)-3-(4-hydroxy-4-(4-(trifluoromethyl)phenyl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24e). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.22g (94%) of **24e** as a white foam as a 93:7 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.24 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.16 – 7.06 (m, 6H), 6.98 – 6.91 (m, 2H), 6.81 (d, *J* = 7.0 Hz, 2H), 5.94 (d, *J* = 9.1 Hz, 1H), 5.89 (d, *J* = 8.1 Hz, 1H), 5.22 (d, *J* = 8.1 Hz, 1H), 5.03 (q, *J* = 8.2 Hz, 1H), 3.53 (s, 1H), 2.56 – 2.70 (m, 2H), 1.51 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 156.7, 152.1, 133.7, 133.6, 128.8 (q, J_{C-F} = 33 Hz), 128.6, 128.5, 128.3, 128.0, 127.4, 126.1, 125.2, 125.1 (q, J_{C-F} = 3.9 Hz), 124.2 (q, J_{C-F} = 272 Hz), 124.1, 117.7, 80.1, 73.2, 66.5, 41.4, 30.0. ^{19}F NMR (565 MHz, $CDCl_3$): – 62.34 ppm. HRMS (DART) m/z calcd for $C_{27}H_{25}F_3NO_3$ $[M + H]^+$: 468.1787; Found $[M + H]^+$: 468.1805.

(4*S*,5*R*)-3-(4-(3-bromophenyl)-4-hydroxypent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24f). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.19 g (79%) of **24f** as a white foam as a 96:4 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.21 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.57 (s, 1H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.22 (t, *J* = 7.9 Hz, 1H), 7.16 – 7.06 (m, 6H), 6.99 – 6.92 (m, 2H), 6.80 (d, *J* = 5.8 Hz, 2H), 6.00 (d, *J* = 9.2 Hz, 1H), 5.88 (d, *J* = 8.1 Hz, 1H), 5.23 (d, *J* = 8.1 Hz, 1H), 5.01 (q, *J* = 8.2 Hz, 1H), 3.25 (s, 1H), 2.64 – 2.54 (m, 2H), 1.45 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 156.7, 150.5, 133.72, 133.70, 129.8, 129.7,

128.54, 128.47, 128.3, 128.1, 128.0, 127.4, 126.1, 124.0, 123.5, 122.5, 117.0, 80.2, 73.1, 66.3, 41.4, 29.9. HRMS (DART) m/z calcd for $C_{26}H_{25}BrNO_3$ $[M + H]^+$: 478.1018; Found $[M + H]^+$: 478.0989.

(4*S*,5*R*)-3-(4-(2-bromophenyl)-4-hydroxypent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24g). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.16g (67%) of **24g** as a white foam as a 97:3 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). Rf = 0.25 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.83 (dd, *J* = 7.9 Hz, 1H), 7.56 (5, *J* = 7.9 Hz, 1H), 7.31 (t, *J* = 7.3 Hz, 1H), 7.15 – 7.06 (m, 7H), 6.92 – 6.99 (m, 2H), 6.82 (d, *J* = 6.2 Hz, 2H), 5.90 (d, *J* = 9.1 Hz, 1H), 5.88 (d, *J* = 8.2 Hz, 1H), 5.24 (d, *J* = 8.2 Hz, 1H), 5.03 (q, *J* = 9.1 Hz, 1H), 3.79 (s, 1H), 3.13 (dd, *J* = 15, 7.6 Hz, 1H), 2.93 (dd, *J* = 15, 7.8 Hz, 1H), 1.70 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 158.9, 145.5, 134.9, 133.8, 133.7, 128.58, 128.57, 128.51, 128.4, 128.2, 128.0, 127.6, 127.5, 126.1, 123.6, 119.8, 118.9, 80.1, 74.3, 65.5, 38.1, 27.5. HRMS (DART) m/z calcd for $C_{26}H_{25}BrNO_3$ $[M + H]^+$: 478.1018; Found $[M + H]^+$: 478.1028.

(4*S*,5*R*)-3-(4-hydroxy-4-(*o*-tolyl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24h). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.15g (75%) of **24h** as a white foam as a 99:1 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). Rf = 0.25 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.43 – 7.37 (m, 1H), 7.17 – 7.05 (m, 9H), 6.98 – 6.91 (m, 2H), 6.79 (d, *J* = 7.0 Hz, 2H), 6.04 (d, *J* = 9.1 Hz, 1H), 5.86 (d, *J* = 8.0 Hz, 1H), 5.21 (d, *J* = 8.0 Hz, 1H), 5.03 (q, *J* = 8.0 Hz, 1H), 2.81 (dd, *J* = 15, 6.9 Hz, 1H), 2.68 (dd, *J* = 15, 7.7 Hz, 1H), 2.66 (s, 1H), 2.50 (s, 3H), 1.55 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.7, 144.6, 135.3, 133.80, 133.79, 132.7, 128.45, 128.40, 128.2, 128.0, 127.4, 127.0, 126.2, 126.15, 126.14, 125.7, 123.8, 117.6, 80.1, 74.8, 66.3, 39.6, 29.2, 22.5. HRMS (DART) m/z calcd for $C_{27}H_{28}NO_3$ $[M + H]^+$: 414.2069; Found $[M + H]^+$: 414.2078.

(4*S*,5*R*)-3-(4-hydroxy-4-(naphthalen-2-yl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24i). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.20 g (88%) of **24i** as a white foam as a 94:6 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.25 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.91 (s, 1H), 7.89 – 7.78 (m, 3H), 7.52 – 7.43 (m, 3H), 7.04 – 7.15 (m, 6H), 6.91 (d, *J* = 6.4 Hz, 2H), 6.77 (d, *J* = 7.3 Hz, 2H), 6.01 (d, *J* = 9.3 Hz, 1H), 5.79 (d, *J* = 8.0 Hz, 1H), 5.13 (d, *J* = 8.0 Hz, 1H), 5.04 (q, *J* = 8.2 Hz, 1H), 3.11 (s, 1H), 2.71 (d, *J* = 7.8 Hz, 2H), 1.58 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.7, 145.2, 133.79, 133.77, 133.2, 132.3, 128.46, 128.48, 128.2, 128.0, 127.9, 127.5, 127.4, 126.14, 126.12, 126.09, 125.8, 123.8, 123.5, 123.3, 117.2, 80.1, 73.7,

66.2, 41.4, 30.0. HRMS (DART) m/z calcd for $C_{27}H_{24}NO_4$ [M-OH]: 426.1700; Found [M-OH] : 426.1708.

(4*S*,5*R*)-3-(4-(benzo[*d*][1,3]dioxol-5-yl)-4-hydroxypent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24j). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.16 g (72%) of **24j** as a pale yellow solid as a 96:4 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). Mp – 187-190 ºC. R_f = 0.25 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.15 – 7.07 (m, 6H), 6.98 – 6.92 (m, 2H), 6.90 (d, *J* = 1.9 Hz, 1H), 6.85 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.80 (d, 6.4 Hz, 2H), 6.75 (d, *J* = 8.1 Hz, 1H), 6.03 (d, *J* = 9.2 Hz, 1H), 5.94 (s, 2H), 5.87 (d, *J* = 8.1 Hz, 1H), 5.25 (d, *J* = 8.0 Hz, 1H), 5.01 (q, *J* = 8.2 Hz, 1H), 2.91 (s, 1H), 2.56 (dd, *J* = 15, 7.7 Hz, 1H), 2.55 (dd, *J* = 15, 7.5 Hz, 1H), 1.44 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.7, 147.6, 146.1, 142.2, 133.80, 133.78, 128.48, 128.42, 128.3, 128.0, 127.4, 126.2, 123.7, 117.8, 117.1, 107.8, 105.9, 100.9, 80.1, 73.4, 66.3, 41.6, 30.1. HRMS (DART) m/z calcd for $C_{27}H_{28}NO_3$ $[M + H]^+$: 414.2069; Found $[M + H]^+$: 414.2078.

(4*S*,5*R*)-3-(4-hydroxy-4-(3-hydroxyphenyl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24k). Prepared according to the general procedure using allenamide **23** and 4 equiv of dimethoxymethylsilane. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.08g (37%) of **24k** as a white foam as a 96:4 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.3 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.18 (t, *J* = 7.9 Hz, 1H), 7.14 – 7.03 (m, 6H), 7.01 (s, 1H), 6.98 – 6.90 (m, 2H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.79 (d, *J* = 6.4 Hz, 2H), 6.73 (dd, *J* = 8.0, 2.6 Hz, 1H), 5.95 (d, *J* = 9.1 Hz, 1H), 5.86 (d, *J* = 8.1 Hz, 1H), 5.51 (s, 1H), 5.14 (d, *J* = 8.0 Hz, 1H), 5.08 (q, *J* = 8.2 Hz, 1H), 3.35 (s, 1H), 2.61 (d, *J* = 7.7 Hz, 2H), 1.49 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.9, 155.8, 149.8, 133.74, 133.68, 129.4, 128.5, 128.4, 128.2, 128.0, 127.4, 126.1, 123.7, 118.3, 117.0, 113.6, 112.2, 80.2, 73.6, 66.4, 41.5, 29.7. HRMS (DART) m/z calcd for $C_{26}H_{26}NO_4$ $[M + H]^+$: 416.1862; Found $[M + H]^+$: 416.1892.

(4*S*,5*R*)-3-(4-hydroxy-4-(5-methylthiophen-2-yl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24l). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.09 g (40%) of **24l** as a white foam as a 90:10 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.25 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.18 – 7.05 (m, 6H), 7.03 – 6.90 (m, 2H), 6.81 (d, *J* = 5.9 Hz, 2H), 6.62 (d, *J* = 1.2 Hz, 1H), 6.56 (d, J = 1.2 Hz, 1H), 6.15 (d, *J* = 9.3 Hz, 1H), 5.87 (d, *J* = 8.0

Hz, 1H), 5.29 (d, *J* = 8.0 Hz, 1H), 5.07 (q, *J* = 8.2 Hz, 1H), 2.89 (s, 1H), 2.66 (dd, *J* = 14, 6.6 Hz, 1H), 2.54 (dd, *J* = 14, 7.9 Hz, 1H), 2.44 (s, 3H), 1.49 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 156.7, 150.5, 138.4, 133.83, 133.76, 128.43, 128.41, 128.2, 128.0, 127.3, 126.2, 124.7, 123.9, 122.1, 115.7, 80.2, 72.8, 66.1, 41.9, 30.1, 15.3. HRMS (DART) m/z calcd for $C_{25}H_{24}NO_2S$ [M-OH]: 402.1522; Found [M-OH] : 402.1498.

(4*S*,5*R*)-3-(4-(furan-2-yl)-4-hydroxypent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24m). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.13 g (67%) of **24m** as a yellow oil as an 80:20 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.25 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 77.35 – 7.31 (m, 1H), 7.15 – 7.06 (m, 6H), 6.99 – 6.93 (m, 2H), 6.82 (d, *J* = 5.8 Hz, 2H), 6.31 – 6.28 (m, 1H), 6.16 (d, *J* = 2.7 Hz, 1H), 6.14 (d, *J* = 9.2 Hz, 1H), 5.89 (d, *J* = 7.9 Hz, 1H), 5.32 (d, *J* = 7.9 Hz, 1H), 5.02 (q, *J* = 8.0 Hz, 1H), 2.86 (s, 1H), 2.73 (dd, *J* = 15, 7.7 Hz, 1H), 2.51 (dd, *J* = 15, 7.8 Hz, 1H), 1.46 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 159.2, 156.7, 141.5, 133.84, 133.76, 128.44, 128.40, 128.2, 128.0, 127.4, 126.2, 123.9, 115.7, 110.1, 104.7, 80.2, 70.7, 66.2, 38.9, 26.8. HRMS (DART) m/z calcd for $C_{24}H_{22}NO_3$ [M-OH]: 372.1594; Found [M-OH] : 372.1574.

(4*S*,5*R*)-3-(4-hydroxy-4-(1-tosyl-1*H*-pyrrol-2-yl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24n). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.2g (81%) of **24n** as a yellow oil as a 96:4 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.28 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.13 – 7.05 (m, 7H), 7.03 (s, 1H), 6.97 – 6.92 (m, 2H), 6.78 (d, *J* = 6.7 Hz, 2H), 6.17 (dd, *J* = 3.3, 1.7 Hz, 1H), 6.05 (d, *J* = 6.9 Hz, 1H), 5.85 (d, *J* = 8.0 Hz, 1H), 5.25 (d, *J* = 8.0 Hz, 1H), 4.96 (q, *J* = 8.4 Hz, 1H), 2.77 (s, 1H), 2.48 (dd, *J* = 15, 7.1 Hz, 1H), 2.43 (dd, *J* = 15, 8.2 Hz, 1H), 2.39 (s, 3H), 1.35 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 156.7, 145.0, 136.8, 136.0, 133.8, 133.7, 130.0, 128.5, 128.4, 128.3, 128.0, 127.3, 126.9, 126.2, 123.7, 121.1, 116.3, 116.2, 111.7, 80.2, 70.5, 66.2, 40.8, 29.1, 21.6. HRMS (DART) m/z calcd for $C_{31}H_{29}N_2O_4S$ [M-OH]: 525.1843; Found [M-OH] : 525.1874.

(4*S*,5*R*)-3-(4-hydroxy-4-(pyridin-3-yl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24o). Prepared according to the general procedure using allenamide **23** and 60 ºC reaction temperature (heated using an oil bath). The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.09g (45%) of **24o** as a white foam as a 94:6

mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.25 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.65 (s, 1H), 8.49 (d, *J* = 4.2 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.15 – 7.05 (m, 7H), 6.95 (d, *J* = 6.9 Hz, 2H), 6.81 (d, *J* = 6.9 Hz, 2H), 5.97 (d, *J* = 9.2 Hz, 1H), 5.89 (d, *J* = 8.1 Hz, 1H), 5.24 (d, *J* = 8.1 Hz, 1H), 5.05 (q, *J* = 8.4 Hz, 1H), 3.54 (s, 1H), 2.65 (d, *J* = 8.1 Hz, 2H), 1.53 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.8, 147.9, 146.8, 143.5, 133.7, 133.6, 132.8, 128.6, 128.5, 128.3, 128.2, 128.0, 127.4, 126.1, 124.2, 123.1, 117.2, 80.2, 72.2, 66.4, 41.4, 29.8. HRMS (DART) m/z calcd for $C_{25}H_{25}N_2O_3$ $[M + H]^+$: 401.1865; Found $[M + H]^+$: 401.1871.

(4*S*,5*R*)-3-(4-(4-(dimethylamino)phenyl)-4-hydroxypent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24p). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.21g (50%) of **24p** as a red foam as a 96:4 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.3 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.25 (d, *J* = 8.7 Hz, 2H), 7.13 – 7.06 (m, 6H), 6.96 – 6.92 (m, 2H), 6.79 (d, *J* = 6.2 Hz, 2H), 6.70 (d, *J* = 8.7 Hz, 2H), 6.11 (d, *J* = 9.3 Hz, 1H), 5.82 (d, *J* = 7.9 Hz, 1H), 5.19 (d, *J* = 7.9 Hz, 1H), 5.01 (q, *J* = 8.5 Hz, 1H), 2.94 (s, 6H), 2.57 (dd, *J* = 15, 7.0 Hz, 1H), 2.52 (dd, *J* = 15, 8.2 Hz, 1H), 2.46 (s, 1H), 1.44 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.7, 149.4, 135.6, 134.0, 133.8, 128.4, 128.2, 128.0, 127.3, 126.9, 126.2, 125.6, 123.4, 116.6, 112.3, 80.2, 73.4, 60.1, 41.5, 40.7, 29.6. HRMS (DART) m/z calcd for $C_{28}H_{31}N_2O_3$ $[M + H]^+$: 443.2335; Found $[M + H]^+$: 443.2364.

(4*S*,5*R*)-3-(4-hydroxy-4-(*p*-tolyl)pent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24q). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.12g (68%) of **24q** as a white foam as a 96:4 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.3 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.28 (d *J* = 7.6 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.16 – 7.05 (m, 6H), 6.98 – 6.92 (m, 2H), 6.80 (d, *J* = 7.0 Hz, 2H), 6.06 (d, *J* = 9.1 Hz, 1H), 5.85 (d, *J* = 8.2 Hz, 1H), 5.22 (d, *J* = 7.9 Hz, 1H), 5.02 (q, *J* = 8.2 Hz, 1H), 2.81 (s, 1H), 2.60 (dd, *J* = 15, 7.2 Hz, 1H), 2.56 (dd, *J* = 15, 8.5 Hz, 1H), 2.36 (s, 3H), 1.48 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.7, 144.9, 136.2, 133.84, 133.78, 128.9, 128.44, 128.40, 128.2, 128.0, 127.4, 126.2, 124.7, 123.6, 117.0, 80.1, 73.5, 66.2, 41.5, 29.9, 21.0. HRMS (DART) m/z calcd for $C_{27}H_{26}NO_2$ [M-OH]: 396.1958; Found [M-OH] : 396.1981.

4-(2-hydroxy-5-((4*S*,5*R*)-2-oxo-4,5-diphenyloxazolidin-3-yl)pent-4-en-2-yl)benzonitrile (24r). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide

0.19g (89%) of **24r** as a yellow oil as a 94:6 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.28 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.18 – 7.05 (m, 6H), 6.97 – 6.91 (m, 2H), 6.80 (d, *J* = 7.1 Hz, 2H), 5.90 (d, *J* = 8.1 Hz, 1H), 5.89 (d, *J* = 8.3 Hz, 1H), 5.22 (d, *J* = 8.1 Hz, 1H), 5.02 (q, *J* = 8.3 Hz, 1H), 3.84 (s, 1H), 2.66 (dd, *J* = 15, 8.3 Hz, 1H), 2.62 (dd, *J* = 15, 8.0 Hz, 1H), 1.51 (s, 3H). ^{13}C{1H} NMR (151 MHz, $CDCl_3$) δ 156.8, 153.7, 133.6, 133.5, 132.1, 128.6, 128.5, 128.3, 128.0, 127.4, 126.1, 125.37, 124.3, 119.0, 118.0, 110.4, 80.2, 73.1, 66.6, 41.3, 29.9. HRMS (DART) m/z calcd for $C_{27}H_{25}N_2O_3$ $[M + H]^+$: 425.1865; Found $[M + H]^+$: 425.1864.

(4*S*,5*R*)-3-(4-hydroxy-4,6-diphenylhex-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24s). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.17g (69%) of **24s** as a pale yellow solid as an 86:14 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). Mp -155-157 ºC R_f = 0.28 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 7.8 Hz, 2H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.245 (t, *J* = 6.7 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.13 – 7.05 (m, 9H), 6.96 – 6.91 (m, 2H), 6.78 (d, *J* = 7.0 Hz, 2H), 5.92 (d, *J* = 9.1 Hz, 1H), 5.86 (d, *J* = 8.1 Hz, 1H), 5.23 (d, *J* = 8.2 Hz, 1H), 5.01 (dt, *J* = 9.0, 6.4 Hz, 1H), 3.31 (s, 1H), 2.73 (dd, *J* = 14, 9.3 Hz, 1H), 2.69 – 2.58 (m, 2H), 2.29 – 2.21 (m, 1H), 2.15 – 2.02 (m, 2H). ^{13}C{1H} NMR (151 MHz, $CDCl_3$) δ 156.8, 145.7, 142.6, 133.8, 133.7, 128.5, 128.40, 128.38, 128.33, 128.2, 128.0, 127.4, 126.6, 126.1, 125.7, 125.4, 125.3, 124.0, 118.2, 80.1, 75.6, 66.4, 45.0, 41.1, 30.0. HRMS (DART) m/z calcd for $C_{32}H_{33}NO_3$ $[M + H]^+$: 490.2382; Found $[M + H]^+$: 490.2410.

(4*S*,5*R*)-3-((*Z*)-3-(1-hydroxy-1,2,3,4-tetrahydronaphthalen-1-yl)prop-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24t). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.18g (83%) of **24t** as a red foam as a 95:5 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.3 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.47 – 7.40 (m, 1H), 7.21 – 7.15 (m, 2H), 7.14 – 7.05 (m, 7H), 6.94 (d, *J* = 6.9 Hz, 2H), 6.78 (d, *J* = 7.2 Hz, 2H), 6.24 (d, *J* = 9.5 Hz, 1H), 5.81 (d, *J* = 7.8 Hz, 1H), 5.20 (d, *J* = 7.8 Hz, 1H), 4.99 (q, *J* = 8.4 Hz, 1H), 2.79 (dt, *J* = 17, 7.0 Hz 1H), 2.72 – 2.59 (m, 3H), 2.41 (dd, *J* = 15, 6.7 Hz, 1H), 1.96 – 1.89 (m, 1H), 1.85 (td, *J* = 11, 2.7 Hz, 2H), 1.66 – 1.57 (m, 1H). ^{13}C{1H} NMR (151 MHz, $CDCl_3$) δ 156.7, 141.9, 136.7, 133.9, 133.7, 128.8, 128.41, 128.40, 128.36, 128.26, 128.0, 127.23, 127.18, 126.3, 126.2, 123.4, 114.2, 80.3, 72.2, 65.8, 39.6, 36.3, 29.6, 19.7. HRMS (DART) m/z calcd for $C_{28}H_{28}NO_3$ $[M + H]^+$: 426.2069; Found $[M + H]^+$: 426.2094.

(4*S*,5*R*)-3-(4-cyclohexyl-4-hydroxypent-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (24u). Prepared according to the general procedure using allenamide **23**. The product was purified by silica gel chromatography (eluent: 20 – 60% EtOAc in hexanes) to provide 0.166 g (82%) of **24u** as a white foam as an 82:18 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). R_f = 0.3 (50% EtOAc/hexanes). Major stereoisomer: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.15 – 7.06 (m, 6H), 6.99 – 6.93 (m, 2H), 6.84 – 6.78 (m, 2H), 6.21 (d, *J* = 9.4 Hz, 1H), 5.90 (d, *J* = 8.1 Hz, 1H), 5.36 (d, *J* = 7.8 Hz, 1H), 5.15 (q, *J* = 8.2 Hz, 1H), 2.32 (dd, *J* = 15, 8.4 Hz, 1H), 2.06 – 2.00 (m, 1H), 2.02 (s, 1H), 1.75 – 1.63 (m, 2H), 1.34 – 1.15 (m, 5H), 1.10 (t, *J* = 13 Hz, 1H), 1.00 (s, 3H) 0.98 – 0.86 (m, 3H). ^{13}C{1H} NMR (151 MHz, $CDCl_3$) δ 156.7, 133.9, 133.8, 128.38, 128.37, 128.2, 128.0, 127.3, 126.2, 123.4, 115.9, 80.2, 73.9, 66.1, 48.5, 36.4, 27.6, 27.1, 26.8, 26.7, 26.5, 23.7. HRMS (DART) m/z calcd for $C_{26}H_{32}NO_3$ $[M + H]^+$: 406.2382; Found $[M + H]^+$: 406.2411.

Branched-selective reductive coupling employing allenamide 23 and acetophenone with IMes as ligand. To a 20 mL crimp-cap vial with stir-bar in an Ar-filled glove-box was charged 2.3 mg (0.013 mmol) of $Cu(OAc)_2$, 5.5 mg (0.016 mmol) of IMes•HCl, and 1.5 mg (0.014 mmol) of KO^{t}Bu. Toluene (0.5 mL) was then added, and the mixture was allowed to stir for 15 min. Allene **23** (83.2 mg, 0.300 mmol) was then added, followed by 29 μL (0.25 mmol) of acetophenone, and the vial was sealed with a crimp-cap septum and removed from the glove-box. Dimethoxymethylsilane (60 μL, 0.5 mmol) was then charged by syringe (***caution: dimethoxymethylsilane should be handled in a well-ventilated fume hood because it is known to cause blindness. Syringes were quenched with 2M NaOH, gas evolution!, prior to disposal)*** at rt, and the mixture was then allowed to stir for 24 h. The reaction was then quenched by the addition of 95 mg of NH_4F and 1.2 mL of MeOH followed by agitation at rt for 30 min – 1 h. To the mixture was then charged 10 mL of 5% $NaHCO_3$ followed by extraction with CH_2Cl_2 (2x5mL). The combined organics were dried with Na_2SO_4 and concentrated *in vacuo*. The crude residue was then dry-loaded onto silica gel using CH_2Cl_2 and purified by flash chromatography on silica gel (eluent: 0–25% EtOAc/Hex) to provide 71.6 mg (72%) of branched product as a white foam as a 92:8 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). Analytically pure material was obtained by recrystallization from EtOAc/hexanes. M.p. 149 – 152 °C. R_f = 0.30 (25% EtOAc/hexanes). ^{1}HNMR ($CDCl_3$, 600 MHz) δ: 7.39 (t, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 7.12 Hz, 1H), 7.26 (s, 1H), 7.09 (t, *J* = 7.12 Hz, 1H), 7.04 (t, *J* = 7.12 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 4H), 6.53 (d, *J* = 7.5 Hz, 2H), 6.30 (br. s, 1H), 6.13 (dt, *J* = 17 Hz, 9.5 Hz, 1H), 6.09 (br. s, 1H), 5.42 (d, *J* = 9.5 Hz, 1H), 5.41 (d, *J* = 8.5 Hz, 1H), 5.14 (d, *J* = 17 Hz, 1H), 5.06 (d, *J* = 8.5 Hz, 1H), 3.55 (d, 9.5 Hz, 1H), 1.42 (s, 3H) ppm. ^{13}CNMR ($CDCl_3$, 126 MHz) δ: 160.1, 145.6, 134.3, 132.5, 130.8, 129.0, 128.5, 128.0, 127.8, 127.7, 126.9, 126.1, 125.4, 121.2, 80.7, 75.9, 68.1, 65.9, 28.9 ppm. HRMS (DART) *m/z* calcd for ($C_{26}H_{25}NO_3$) $[M+H]^+$: 400.1800; Found $[M+H]^+$: 400.1891.

One-gram scale reactions. The scale-up of **15q** using Method A was reported previously.[5] Method B: To a 25 mL Schlenk flask with stir-bar was charged 135 mg (0.746 mmol) of $Cu(OAc)_2$ and 0.578 g (0.894 mmol) of ligand **L5** and the flask was sealed with a septum an inerted with Ar using vacuum-purge cycles (3x). To the Schlenk flask was then charged 10 mL of toluene, and the mixture was stirred for 10 min. To a separate 50 mL Schlenk flask was charged allene **23** (2.48 g, 8.94 mmol) and the flask was sealed with a septum and inerted with Ar using vacuum-purge cycles (3x). The ketone (1.00 g, 1.00 mL, 7.45 mmol) was then charged by syringe. To the ketone/allene Schlenk flask was then charged the Cu-catalyst solution by canula addition. The residue in the catalyst containing Schlenk flask was then rinsed over using an additional 4.9 mL of toluene, again using canula transfer by Ar pressure. The resultant mixture was then cooled in an ice bath, and dimethoxymethylsilane (1.84 mL, 1.58 g, 14.9 mmol) was charged by syringe (***caution: dimethoxymethylsilane should be handled in a well-ventilated fume hood because it is known to cause blindness. Syringes were quenched with 2M NaOH, gas evolution!, prior to disposal)***. The mixture was then allowed to warm to rt and stirred for 24 h. The reaction was then transferred to a larger flask containing 2.76 g (74.5 mmol) of NH_4F and 30 mL of MeOH, and the mixture was agitated for 2 h. The mixture was then concentrated *in vacuo* to remove ~30 mL of volatiles and then 40 mL of 5% $NaHCO_3$ was charged. The mixture was then extracted with CH_2Cl_2 (3x30mL), and the combined organics were dried with Na_2SO_4 and concentrated *in vacuo*. The crude residue was then dry-loaded on to silica gel using CH_2Cl_2 and purified by flash chromatography (gradient, 20 – 60% EtOAc in hexanes) to afford 2.37 g (77%) of *l*-**24q** in 95:5 dr (determined by ^{1}HNMR spectroscopic analysis).

Synthesis of 26 from *l*-15q. To a solution of 0.150 g (0.445 mmol) of **15q** in 1.8 mL of THF at – 5 ºC was charged 0.120 g (0.533 mmol) of *N*-iodosuccinimde under N_2. The mixture was stirred at this temperature for 1.5 h, at which time, the starting material was consumed by TLC analysis. To the reaction was added 2 mL of 10% $Na_2S_2O_3$ and 2 mL of water, and the mixture was extracted with MTBE (3x4mL). The combined organic layers were then washed with water (2x5mL) to remove succinimide, and then dried with anhydrous Na_2SO_4 and concentrated *in vacuo* to obtain a white foam. The crude residue was then dissolved in 2.0 mL of MTBE under N_2 and cooled to – 20 ºC. *n*-BuLi (0.19 mL, 2.5M in hexanes, 0.48 mmol) was then added dropwise, and the mixture was then allowed to stir at this temperature for 15 min to consume the iodointermediate (TLC analysis). The reaction was quenched by the addition of 0.6 mL of 2M HCl followed by the addition of 2 mL of water, and the mixture was extracted with CH_2Cl_2 (3x3mL). The combined organics were dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was then triturated with 5 mL of 5% MTBE in hexanes, and the formed solid was isolated by filtration washing with 5% MTBE in hexanes (2x5mL) followed by hexanes (2x5mL). The solid was further dried *in vacuo* to afford 62.3 mg (86%) of recovered Evans oxazolidinone (**27a**). The filtrate was then concentrated *in vacuo*, and the crude residue purified by flash chromatography on silica gel (gradient, hexanes to 5% EtOAc in hexanes) to afford 70.0 mg (90%) of **26** as a colorless oil. R_f = 0.50 (5 % EtOAc/hexanes). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (d, J = 8.0 Hz, 2H), 7.15 (d, J =

8.0 Hz, 2H), 6.38 (q, J = 1.8 Hz, 1H), 4.84 (q, J = 1.8 Hz, 1H), 2.81 (dt, J = 15 Hz, 1.8 Hz, 1H), 2.75 (dt, J = 15 Hz, J = 1.8 Hz, 1H), 2.34 (s, 3H), 1.64 (s, 3H). $^{13}C\{1H\}$ NMR (151 MHz, $CDCl_3$) δ 144.8, 144.2, 136.3, 128.9, 124.4, 98.5, 87.2, 44.2, 29.1, 21.0. HRMS (DART) *m/z* calcd for $C_{12}H_{15}O$ $[M + H]^+$: 175.1123; Found $[M + H]^+$: 175.1151.

Synthesis of lactol 29. To a solution of 59.8 mg (0.343 mmol) of dihydrofuran **26** in 1.4 mL of 1:1 THF:H_2O at ambient temperature was charged 0.49 mL (8.6 mmol) of acetic acid, and the mixture was allowed to stir at rt and monitored by HPLC. The starting material was consumed after 8 h, and the mixture was then poured in to 5 mL of satd. $NaHCO_3$ solution and extracted with MTBE (3x5mL). The combined organic layers were then washed with satd. $NaHCO_3$ solution (3x5mL), and then dried with anhydrous Na_2SO_4 and concentrated *in vacuo* to obtain 65.5 mg (99%) of lactol **29** as a colorless oil. The material was spectroscopically identical to that obtained previously.[5]

Synthesis of (S)-boivinianin A (28). The synthesis of **28** from lactol **29** has been reported previously.[5] The synthesis of **28** from **26** using PCC was adapted from the literature.[21] To a solution of 20.6 mg (0.118 mmol) of dihydrofuran **26** in 0.52 mL of CH_2Cl_2 was charged 51.0 mg (0.236 mmol) of PCC. After consumption of the starting material (1 h, TLC analysis), 3 mL of MTBE was charged, and the mixture was filtered through celite. The black residue in the flask was then triturated with MTBE (3 mL) and passed through the celite bed. This trituration was then repeated two additional times. The combined filtrate was then concentrated *in vacuo* and the crude residue was purified through a short pad of silica gel eluting with CH_2Cl_2 followed by 3% EtOAc in CH_2Cl_2. Concentration of the combined fractions afforded 20.5 mg (91%) of **28** as a colorless oil. The material was spectroscopically identical to that obtained previously.[5] R_f = 0.36 (CH_2Cl_2).

Synthesis of 30. The synthesis of **30** was performed using a literature protocol.[22] To a solution of 18.6 mg (0.0983 mmol) of lactol **29** and 46.9 μL (0.295 mmol) of allyl trimethylsilane in 0.66 mL of CH_2Cl_2 at – 78 ºC was charged 10 μL (0.05 mmol) of a freshly prepared 0.5 M solution of I_2 in CH_2Cl_2. The mixture was allowed to stir at – 78 ºC for 1 h and then slowly warmed to rt. The resultant mixture was then held at rt for an additional 2.5 h to consume the starting material (TLC analysis). Water (1 mL) and 10% $Na_2S_2O_3$ (0.5 mL) was charged, and the mixture was extracted with CH_2Cl_2 (2x3mL). The combined organics were then dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. Analysis of the crude material by ^{1}HNMR spectroscopy showed a 75:25 mixture of diastereomers. The crude residue was then purified by flash chromatography on silica gel (gradient, hexanes to 4% EtOAc in hexanes) to afford 20.0 mg (94%) of **30** as a colorless oil as a 75:25 mixture of diastereomers (determined by ^{1}HNMR spectroscopic analysis). Assignment of the major diastereomer as the *trans*-isomer was based off of comparison of the ^{1}HNMR chemical shift values to similar compounds in the literature.[28] R_f = 0.27 (4% EtOAc

in hexanes). Major diastereomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 5.82 – 5.92 (m, 1H), 5.10 (d, *J* = 18 Hz, 1H), 5.05 (d, *J* = 10 Hz, 1H), 4.20 (p, *J* = 6.6 Hz, 1H), 2.42 – 2.50 (m, 1H), 2.33 (s, 3H), 2.14 – 2.29 (m, 2H), 1.99 – 2.09 (m, 2H), 1.52 – 1.58 (m, 1H), 1.49 (s, 3H). ^{13}C{1H} NMR (151 MHz, $CDCl_3$) δ 146.1, 135.7, 135.2, 128.6, 124.7, 116.7, 84.3, 78.7, 40.7, 39.9, 31.1, 29.9, 20.9. Minor diastereomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 5.82 – 5.92 (m, 1H), 5.03 – 5.15 (m, 2H), 4.05 (p, *J* = 6.3 Hz, 1H), 2.42 – 2.50 (m, 1H), 2.33 (s, 3H), 2.29 – 2.36 (m, 1H), 2.14 – 2.22 (m, 1H), 1.99 – 2.08 (m, 1H), 1.80 – 1.89 (m, 1H), 1.63 – 1.72 (m, 1H), 1.51 (s, 3H). ^{13}C{1H} NMR (151 MHz, $CDCl_3$) δ 145.4, 135.7, 135.0, 128.8, 124.6, 116.8, 84.4, 78.0, 40.6, 39.1, 30.8, 30.6, 20.9. HRMS (DART) *m/z* calcd for $C_{15}H_{21}O$ $[M + H]^+$: 217.1592; Found $[M + H]^+$: 217.1617.

ASSOCIATED CONTENT

Supporting Information

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

Copies of ^{1}H and ^{13}C NMR spectra of all new compounds.

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Notes

The authors declare no competing financial interest.

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Generic License has already been assigned to the Author Accepted Manuscript version that might arise from this submission. We thank Dr. Joseph Turner (VCU) for assistance in collecting HRMS data.

References

[1] Reviews: (a) Nguyen, K. D.; Park, B. Y.; Luong, T.; Sato, H.; Garza, V. J.; Krische, M. J. Metal-Catalyzed Reductive Coupling of Olefin-Derived Nucleophiles: Reinventing Carbonyl Addition. *Science* **2016**, *354*, 300 – 305. (b) Hassan, A.; Krische, M. J. Unlocking Hydrogenation for C-C Bond Formation: A Brief Overview of Enantioselective Methods. *Org. Process Res. Dev.* **2011**, *15*, 1236 – 1242. (c) Han, S. B.; Kim, I. S.; Krische, M. J. Enantioselective Iridium-Catalyzed Carbonyl Allylation from the Alcohol Oxidation Level *via* Transfer Hydrogenation: Minimizing Pre-activation for Synthetic Efficiency. *Chem. Commun.* **2009**, 7278 – 7287. (d) Holmes, M.; Schwartz, L. A.; Krische, M. J. Intermolecular Metal-Catalyzed Reductive Coupling of Dienes, Allenes, and Enynes with Carbonyl Compounds and Imines. *Chem. Rev.* **2018**, *118*, 6026 – 6052. (e) Xiang, M.; Pfaffinger, D. E.; Krishce, M. J. Allenes and Dienes as Chiral Allylmetal Pronucleophiles in Catalytic Enantioselective C=X Addition: Historical Perspective and State-of-The-Art Survey. *Chem. Eur. J.* **2021**, *27*, doi.org/10.1002/chem.202101890. (f) Agrawal, T.; Sieber, J. D. Recent Developments in C-C Bond Formation Using Catalytic Reductive Coupling Strategies. *Synthesis* **2020**, *52*, 2623 – 2638.

[2] For selected reviews, see: (a) Yus, M.; Gonzalez-Gomez, J. C.; Foubelo, F. Diastereoseelctive Allylation of Carbonyl Compounds and Imines: Application to the Synthesis of Natural Products. *Chem. Rev.* **2013**, *113*, 5595 – 5698. (b) Yus, M.; Gonzalez-Gomez, J. C.; Foubelo, F. Catalytic Enantioselective Allylation of Carbonyl Compounds and Imines. *Chem. Rev.* **2011**, *111*, 7774 – 7854. (c) Denmark, S. E.; Fu, J. Catalytic Enantioselective Addition of Allylic Organometallic Reagents to Aldehydes and Ketones. *Chem. Rev.* **2003**, *103*, 2763 – 2793. (d) Huo, H. –X.; Duvall, J. R.; Huang, M. –Y.; Hong, R. Catalytic Asymmetric Allylation of Carbonyl Compounds and Imines with Allylic Boronoates. *Org. Chem. Front.* **2014**, *1*, 303 – 320. (e) Tietze, L. F.; Kinzel, T.; Brazel, C. C. The Domino Multicomponent Allylation Reaction for the Stereoselective Synthesis of Homoallylic Alcohols. *Acc. Chem. Res.* **2009**, *42*, 367 – 378. (f) Yamamoto, H.; Wadamoto, M. Silver-Catalyzed Asymmetric Allylation: Allyltrimetoxysilane as a Remarkable Reagent. *Chem. – Asian J.* **2007**, *2*, 692 – 698. (g) Srebnik, M.; Ramachandran, P. V. The Utility of Chiral Organoboranes in the Preparation of Optically Active Compounds. *Aldrichimica Acta* **1987**, *20*, 9 – 24.

[3] Selected examples: (a) Zhang, W.; Chen, W.; Xiao, H.; Krische, M. J. Carbonyl *anti*-(α-amino)allylation via Ruthenium Catalyzed Hydrogen Autotransfer: Use of an Acetylenic Pyrrole as an Allylmetal Pronucleophile. *Org. Lett.* **2017**, *19*, 4876 – 4879. (b) Nguyen, K. D.; Herkommer, D.; Krische, M. J. Ruthenium-BINAP Catalyzed Alcohol C-H *tert*-Prenylation via 1,3-Enyne Transfer Hydrogenation: Beyond Stoichiometric Carbanions in Enantioselective

Carbonyl Propargylation. *J. Am. Chem. Soc.* **2016**, *16*, 5238 – 5241. (c) Grayson, M. N.; Krische, M. J.; Houk, K. N. Ruthenium-Catalyzed Asymmetric Hydroxyalkylation of Butadiene: The Role of the Formyl Hydrogen Bond in Stereochemical Control. *J. Am. Chem. Soc.* **2015**, *137*, 8838 – 8850. (d) Liang, T.; Nguyen, K. D.; Zhang, W.; Krische, M. J. Enantioselective Ruthenium-Catalyzed Carbonyl Allylation via Alkyne-Alcohol C-C Bond-Forming Transfer Hydrogenation: Allene Hydrometalation vs Oxidative Coupling. *J. Am. Chem. Soc.* **2015**, *137*, 3161 – 3164. (e) McInturff, E. L.; Yamaguchi, E.; Krische, M. J. Chiral-Anion-Dependant Inversion of Diastereo- and Enantioselectivity in Carbonyl Crotylation via Ruthenium-Catalyzed Butadiene Hydroxylation. *J. Am. Chem. Soc.* **2012**, *134*, 20628 – 20631. (f) Leung, J. C.; Geary, L. M.; Chen, T. –Y.; Zbieg, J. R.; Krische, M. J. Direct, Redox-Neutral Prenylation and Geranylation of Secondary Carbinol C-H Bonds: C4-Regioselectivity in Ruthenium-Catalyzed C-C Couplings of Dienes and α-Hydroxy Esters. *J. Am. Chem. Soc.* **2012**, *134*, 15700 – 15703. (g) Ng, S. –S.; Jamison, T. F. Highly Enantioselective and Regioselective Nickel-Catalyzed Coupling of Allenes, Aldehydes, and Silanes. *J. Am. Chem. Soc.* **2005**, *127*, 7320 – 7321. (h) Song, M.; Montgomery, J. Nickel-Catalyzed Couplings and Cyclizations Involving Allenes, Aldehydes, and Organozincs. *Tetrahedron* **2005**, *61*, 11440 – 11448. (i) Ng, S. –S.; Jamison, T. F. Enantioselective and Regioselective Nickel-Catalyzed Multicomponent Coupling of Chiral Allenes, Aromatic Aldehydes, and Silanes. *Tetrahedron* **2005**, *61*, 11405 – 11417.

[4] (a) Tsai, E. Y.; Liu, R. Y.; Yang, Y.; Buchwald, S. L. A Regio- and Enantioselective CuH-Catalyzed Ketone Allylation with Terminal Allenes. *J. Am. Chem. Soc.* **2018**, *140*, 2007 – 2011. (b) Liu, R. Y.; Zhou, Y.; Yang, Y.; Buchwald, S. L. Enantioselective Allylation Using Allene, a Petroleum Cracking Byproduct. *J. Am. Chem. Soc.* **2019**, *141*, 2251 – 2256. (c) Liu, T. Y.; Yang, Y.; Buchwald, S. L. Regiodivergent and Diastereoselective CuH-Catalyzed Allylation of Imines with Terminal Allenes. *Angew. Chem. Int. Ed.* **2016**, *55*, 14077 – 14080. (d) Li, C.; Liu, R. Y.; Jesikiewicz, L. T.; Yang, Y.; Liu, P.; Buchwald, S. L. CuH-Catalyzed Enantioselective Ketone Allylation with 1,3-Dienes: Scope, Mechanism, and Applications. *J. Am. Chem. Soc.* **2019**, *141*, 5062 – 5070. (e) Li, C.; Shin, K. Liu, R. Y.; Buchwald, S. L. Engaging Aldehydes in CuH-Catalyzed Reductive Coupling Reactions: Stereoselective Allylation with Unactivated 1,3-Diene Pronucleophiles. *Angew. Chem. Int. Ed.* **2019**, *58*, 17074 – 17080.

[5] Klake, R. K.; Gargaro, S. L.; Gentry, S. L.; Elele, S. O.; Sieber, J. D. Development of a Strategy for Linear-Selective Cu-Catalyzed Reductive Coupling of Ketones and Allenes for the Synthesis of Chiral γ-Hydroxyaldehyde Equivalents. *Org. Lett.* **2019**, *21*, 7992 – 7998.

[6] Gao, S.; Chen, M. α-Silicon Effect Assisted Curtin-Hammett Allylation Using Allylcopper Reagents Derived from 1,3-Dienylsilanes. *Chem. Sci.* **2019**, *10*, 7554 – 7560.

[7](a) Gargaro, S. L.; Klake, R. K.; Burns, K. L.; Elele, S. O.; Gentry, S. L.; Sieber, J. D. Access to a Catalytically Generated Umpolung Reagent through the Use of Cu-Catalyzed Reductive Coupling of Ketones and Allenes for the Synthesis of Chiral Vicinal Aminoalcohol Synthons. *Org. Lett.* **2019**, *21*, 9753 – 9758. (b) Klake, R. K.; Edwards, M. D.; Sieber, J. D. Synthesis of 1,2-Aminoalcohols through Enantioselective Aminoallylation of Ketones by Cu-Catalyzed Reductive Coupling. *Org. Lett.* **2021**, *23*, 6444 – 6449. (c) Agrawal, T.; Martin, R. T.; Collins, S.; Wilhelm, Z.; Edwards, M. D.; Gutierrez, O.; Sieber, J. D. Access to Chiral Diamine Derivatives through Stereoselective Cu-Catalyzed Reductive Coupling of Imines and Allenamides. *J. Org. Chem.* **2021**, *86*, 5026 – 5046.

[8] Zheng, M.; Chen, P.; Huang, L.; Wu, W.; Jiang, H. Nucleo-Palladation-Triggering Alkene Functionalization: A Route to γ-Lactones. *Org. Lett.* **2017**, *19* (21), 5756–5759.

[9] Spielmann, K.; Xiang, M.; Schwartz, L. A.; Krische, M. J. Direct Conversion of Primary Alcohols to 1,2-Amino Alcohols: Enantioselective Iridium-Catalyzed Carbonyl Reductive Coupling of Phthalimido-Allene via Hydrogen Auto-Transfer. *J. Am. Chem. Soc.* **2019**, *141* (36), 14136–14141.

[10] Both the (*R*)- and (*S*)-enantiomers of 4-phenyl-2-oxazolidinone (Evans' oxazolidinone) are commercially available at a cost of ~$0.25/gram on 1 kg scale (Combi-Blocks/Oakwood Chemical, Nov. 16, 2020). The allenamide is made in one step from 4-phenyl-2-oxazolidinone, see: Bousfield, T. W.; Kimber, M. C. A simple one-pot preparation of *N*-allenyl amides, ureas, carbamates, and sulfonamides using a DMSO/^{t}BuOK protocol. *Tetrahedron Lett.* **2015**, *56*, 350 – 352.

[11] a) Tolman, C. A. Steric Effects of Phosphorous Ligands in Organometallic Chemistry and Homogeneous Catalysis. *Chem. Rev.* **1977**, *77*, 313 – 348. (b) Dorta, R.; Stevens, E. D.; Scott, N. M.; Costabile, C.; Cavallo, L.; Hoff, C. D.; Nolan, S. P. Steric and Electronic Properties of N-Heterocyclic Carbenes (NHC): A Detailed Study on Their Interactions with $Ni(CO)_4$. *J. Am. Chem. Soc.* **2005**, *127*, 2485 – 2495.

[12] Bull, S. D.; Davies, S. G.; Jones, S.; Polywka, M. E. C.; Prasad, R. S.; Sanganee, H. J. A Practical Procedure for the Multigram Synthesis of the SuperQuat Chiral Auxiliaries. *Synlett* **1998**, 519 – 521.

[13] 2-amino-1,2-diphenylethanol prices at 500 g scale: (a) (1*R*, 2*S*)-enantiomer $1.68/gram; (b) (1*S*, 2*R*)-enantiomer $1.56/gram (Combi-Blocks, March 25, 2021).

[14] Allenamide **23** was stored on the bench-top under an air atmosphere and monitored by quantitative ^{1}HNMR spectroscopy relative to dimethylfumarate as analytical standard. No loss in purity was observed after nine months. In contrast, allenamide **13** is a yellow oil that can be held for up to six months without degradation if stored below – 20 ºC.

[15] Tris(2,4-di-tert-butylphenyl) phosphite (**L5**) is available on 500 g scale at a price of $0.21/g from the Aldrich Chemical Company (August 24, 2021).

[16] Catalyst prices from Strem Chemical Company (Aug. 24, 2021): $Cu(OAc)_2$ $1.60/g at 100 g scale.

[17] Based on these results allenamide **23** was examined under branched-selective conditions (ref. 7a) utilizing IMes as ligand resulting in 78:22 *b*:*l* selectivity and 72% yield of branched product in 92:8 dr. These results show no improvements.

[18] Borrajo-Calleja, G. M.; Bizet, V.; Burgi, T.; Mazet, C. Access to Enantioenriched 2,3- and 2,5-Dihydrofurans with a fully substituted C2 Stereocenter by Pd-Catalyzed Asymmetric Intermolecular Heck Reaction. *Chem. Sci.* **2015**, *6*, 4807 – 4811.

[19] (a) Yang, B.; Zhu, C.; Qiu, Y.; Backvall, J. -E. Enzyme and Ruthenium-Catalyzed Enantioselective Transformation of a-Allenic Alcohols into 2,3-Dihydrofurans. *Angew. Chem. Int. Ed.* **2016**, *55*, 5568 – 5572. (b) Jalali-Naini, M.; Lallemand, J. Y. Iodocyclisation of Unsaturated Lactols and Acetals. A New Route to Furo-2,3b-Furans and Pyrans. *Tetrahedron Lett.* **1986**, *27*, 497 – 500. (c) Hodgson, D. M.; Stent, M. A. H.; Wilson, F. X. Organolithium-Induced Synthesis of Unsaturated Diols from Epoxides of Dihydrofurans and Dihydropyrans. *Synthesis* **2002**, 1445 – 1453.

[20] (a) Boger, D. L.; Ichikawa, S.; Zhong, W. Total Synthesis of Fostriecin (CI-920). *J. Am. Chem. Soc.* **2001**, *123*, 4161 – 4167. (b) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. Catalytic Asymmetric Dihydroxylation. *Chem. Rev.* **1994**, *94*, 2483 – 2547.

[21] Piancatelli, G.; Scettri, A.; D'Auria, M. Pyridinium Chlorochromate in the Organic Synthesis: a Convenient Oxidation of Enol-ethers to Esters and Lactones *Tetrahedron Lett.* **1977**, 3483 – 3484.

[22] Yadav, J. S.; Reddy, B. V. S.; Reddy, A. S.; Reddy, C. S.; Raju, S. S. Highly Diastereoselective Allylation of Lactols and Their Ethers Using Molecular Iodine *Tetrahedron Lett.* **2009**, *50*, 6631 – 6634.

[23] Lang. K.; Park. J.; Hong. S. Development of Bifunctional Aza-Bis(oxazoline) Copper Catalysts for Enantioselective Henry Reaction. *J. Org. Chem*. **2010**, 75, 19, 6424–6435.

[24] Jiang, B.; Xu, M. Catalytic Diastereoselective Puson-Khand Reaction: and Efficient Route to Enantiopure Cyclopenta[*c*]proline Derivatives. *Org. Lett.* **2002**, *4*, 4077 – 4080.

[25] Monbaliu. J-C.; Tinant. B.; Marchand-Brynaert. J. Reactivity of (R)-4-phenyloxazolidine-2-thione chiral auxiliary: from deprotection to heterocyclic interconversion. *Heterocycles* **2008**, *75*, 2459-2475.

[26] Volpe, R.; Lepage, R. J.; White, J. M.; Krenske, E. H.; Flynn, B. L. Asymmetric synthesis of multiple quaternary stereocenter-containing cyclopentyls by oxazolidinone-promoted Nazarov cyclizations. *Chem. Sci*. **2018**, *9*, 4644 – 4649.

[27] Wei, L. -L.; Hsung, R. P.; Xiong, H.; Mulder, J. A.; Nkansah, N. T. First Stereoselective Inverse Demand [4 + 2] Cycloaddition Reactions of Novel Chiral Allenamides with Heterodienes. Preparation of Highly Functionalized 2-Arylpyranyl Heterocycles. *Org. Lett.* **1999**, *1*, 2145 – 2148.

[28] (a) Schmitt, A.; Reibig, H. -U. On the Stereoselectivity of γ-Lactol Substitutions with Allyl- and Propargylsilanes – Synthesis of Disubstituted Tetrahydrofuran Derivatives. *Eur. J. Org. Chem.* **2000**, 3893 – 3901. (b) Pilli, R. A.; Riatto, V. B. Diastereoselective Synthesis of 2,5-disubstituted Tetrahydrofuran Derivatives. *Tetrahedron Asymm.* **2000**, *11*, 3675 – 3686.