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TANDEM PALLADIUM-CATALYZED ALLENE ARYLATION AND OXAZOLINE FORMATION[§]

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[§]*Dedicated to Prof. Barry M. Trost, outstanding scientist and inspiring mentor, on the occasion of his 65th birthday.*

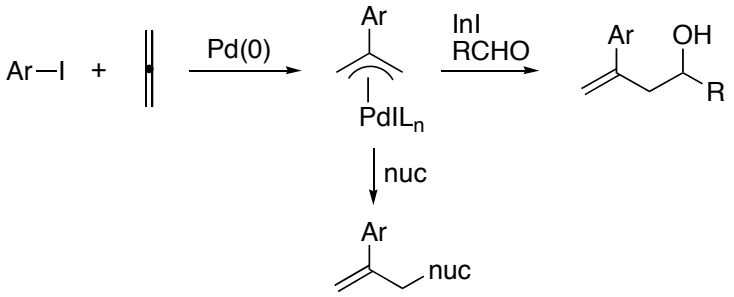
Abstract – The tandem palladium-catalyzed addition of aryl iodides to allenes followed by cyclization to afford oxazolines was investigated. A variety of chiral 5-vinyloxazolines were obtained in high yield with excellent stereoselectivity *via* equilibration of the intermediate π-allylpalladium complex.

INTRODUCTION

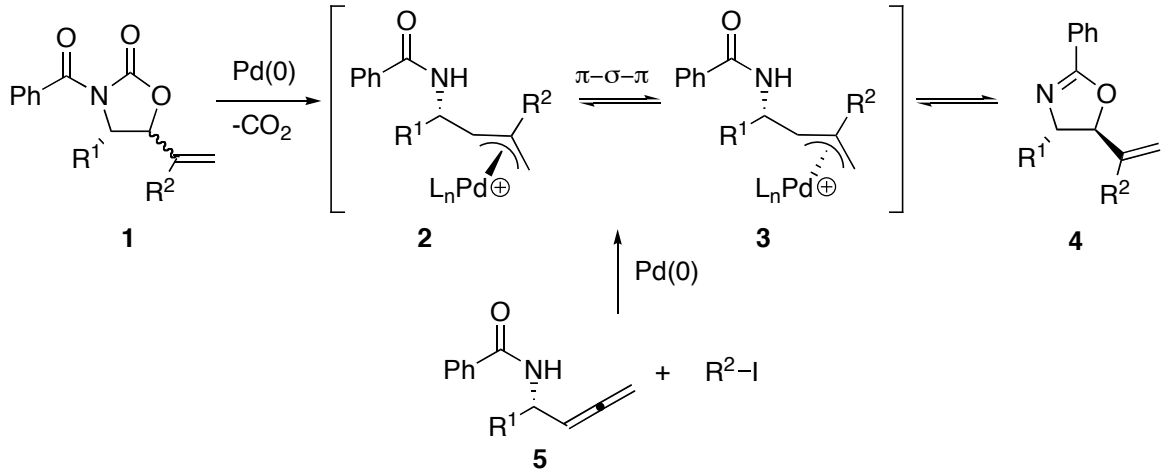
The efficient synthesis of natural products and highly functionalized chiral building blocks demands the design of atom economical[1] approaches. One strategy for optimizing atom economy is the development of tandem reaction cascades that effect more than one synthetic transformation in a single reaction pot.[2] Palladium-catalyzed cascade sequences have played a significant role in this regard. The Pd(0)-catalyzed arylation of allenes has been employed for tandem reactions as they produce *in situ* a π-allyl palladium intermediate that can be intercepted with appropriate nucleophiles or utilized in umpolung allylations of aldehydes (Scheme 1).[3] These multicomponent coupling processes allow for efficient synthesis of more functionalized compounds from relatively simple starting materials.

Recent work from our laboratory has highlighted the efficacy of Pd(0)-catalyzed oxazoline formation from 5-vinyloxazolidinones with thermodynamic equilibration via dynamic π-allylpalladium complexes (Scheme 2).[4,5] Thus, oxazolidinones (**1**) readily convert into oxazolines (**4**) with high levels of diastereoselectivity *via* rapidly isomerizing intermediates (**2**) and (**3**). The thermodynamic equilibration relies upon the reversible nature of the cyclization reaction. We have established that these chiral oxazolines are useful intermediates for the synthesis of a variety of biologically important targets

including balanol,[6] lactacystin,[7] sphingolipids,[8] and inhibitors for matrix metalloproteinases.[9] We envisioned that the same π-allylpalladium intermediates (**2**) and (**3**) could be generated via the Pd(0)-catalyzed addition of aryl iodides (R^2 = aryl) to chiral aminoallenes (**5**). This tandem reaction would afford a facile and efficient route to diversely substituted oxazolines (**4**) as a large number of different aryl groups could be incorporated into the coupling reaction. Herein we disclose the results of our study of the tandem allene arylation/oxazoline formation sequence.



Scheme 1. Tandem allene arylation/π-allyl interception strategies

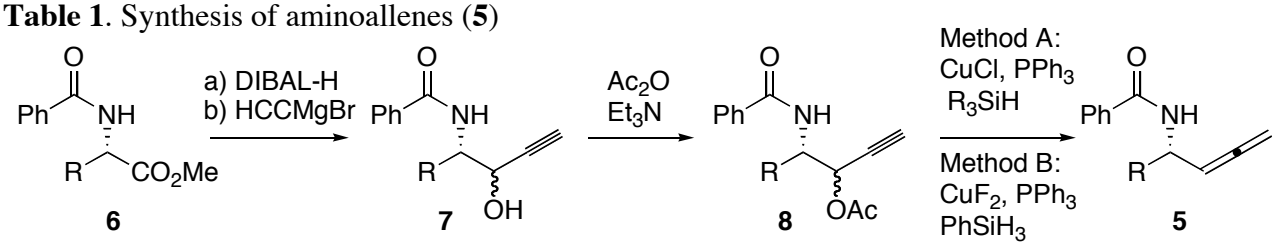


Scheme 2. Pd(0)-Catalyzed oxazoline formation

RESULTS AND DISCUSSION

We began by synthesizing the required allenes from commercially available α-amino acids. The allene substrates (**5**) for this study were prepared as summarized in Table 1. Starting from amino acid derivatives (**6**), DIBAL-H reduction followed by addition of magnesium acetylide afforded the propargylic alcohols (**7**).[10] These were obtained as a mixture of diastereomers ranging from 70:30 to 90:10, *syn:anti*. Acylation with acetic anhydride gave the propargylic acetates (**8**) which were then subjected to reduction *via* S_N2' substitution with copper hydride reagents[11] to give the chiral allenes (**5**) in good yield.

Table 1. Synthesis of aminoallenes (**5**)

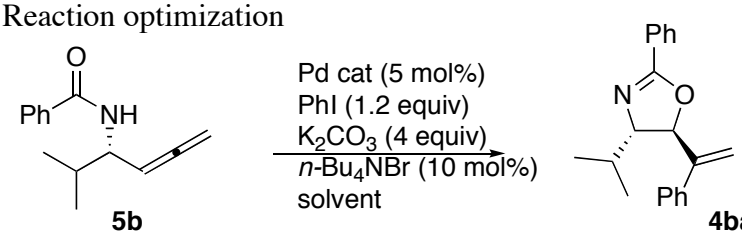


entry		R	yield of **7**[a]	*syn:anti*[b]	yield of **8**[a]	yield of **5**[a] (method)
1	**a**	Ph	75%	70:30	75%	60% (A) 54% (B)
2	**b**		73%	90:10	67%	67% (A)
3	**c**		56%	70:30	88%	70% (B)
4	**d**		41%	70:30	86%	75% (B)
5	**e**	H_3C	82%	80:20	92%	58% (B)

[a]Isolated yield. [b]Measured by ^{1}H NMR spectroscopy.

With allenes (**5**) in hand, we explored the reaction conditions to find a suitable catalyst and solvent. Utilizing the allene (**5b**) and iodobenzene as the aryl partner, the Pd-catalyzed allene arylation/cyclization was investigated and the results are shown below in Table 2.[12] Optimal reaction was found employing $Pd(PPh_3)_4$ as the catalyst in acetonitrile at reflux. This resulted in 70% isolated yield of (**4b**) as a single diasteromer by ^{1}H NMR spectroscopy (entry 1). The phase transfer catalyst, *n*-Bu_4NBr, was important for successful catalytic turnover as the yield dropped significantly when it was not used (entry 2). Interestingly, the halogen of the aryl group was important for both reactivity as well as diastereoselectivity. When bromobenzene was employed in the reaction (entry 3), the yield fell to 45% and the selectivity dropped to 85:15, *trans:cis*. Presumably, the nature of halide ligand on the π-allylpalladium intermediate exerted an influence on how rapidly it underwent allyl isomerization relative to cyclization.[13] The bidentate bisphospine ligand, dppp, was also not very effective for the reaction. Although stereocontrol was complete, the yields were low (entries 4 and 5). The more electron rich ligand, P(*t*-Bu)$_3$ behaved similarly and generally afforded less than 50% isolated yield of oxazoline (not shown). Acetonitrile was the best solvent tested. As shown in entries 6-8, lower yields and lower selectivity was observed when the reaction was carried out in other solvents. In toluene, good diastereoselectivity was obtained, however, the yield was only 36%. When run in dioxane the reaction was very poor affording only 11% isolated yield with nearly equal mixture of diastereomers. Thus, reversible cyclization/allyl isomerization appeared to be best in acetonitrile.

Table 2. Reaction optimization



5b **4ba**

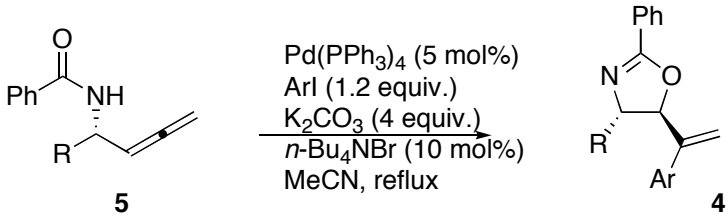
entry	catalyst/ligand	solvent	T (°C)	t (h)	% yield[a]	*trans:cis*[b]
1	$Pd(PPh_3)_4$	MeCN	81	24	70	>99:1
2[c]	$Pd(PPh_3)_4$	MeCN	81	48	41	>99:1
3[d]	$Pd(PPh_3)_4$	MeCN	81	24	45	85:15
4	$Pd_2(dba)_3$•$CHCl_3$/dppp	MeCN	81	24	44	>99:1
5[c]	$Pd_2(dba)_3$•$CHCl_3$/dppp	THF	40	48	11	>99:1
6	$Pd(PPh_3)_4$	toluene	90	36	36	>99:1
7	$Pd(PPh_3)_4$	DMF	90	36	25	90:10
8	$Pd(PPh_3)_4$	dioxane	90	36	19	60:40

[a]Isolated yield. [b]Measured by ^{1}H NMR spectroscopy. [c]No *n*-Bu_4NBr. [d]PhBr used instead of PhI.

Utilizing the best conditions for arylation and cyclization, we next examined the scope of the reaction with substrates (**5a-e**) and a variety of aryl iodides. The results of this study are summarized in Table 3. In general yields were good to excellent and the diastereoselectivity was completely controlled in most cases. While it was expected that substrates with larger R substituents would thermodynamically favor the *trans* isomer solely, we were delighted to find that even when R=Me (entries 16-20) excellent diastereoselectivity was obtained. The only cases where a mixture of diastereomers was produced occurred when thiophene was used as the aryl coupling partner. In these cases, selectivity ranged from 63:37 to 92:8 (entries 3, 6, 9, and 13). This could be due coordination of the palladium to the thiophene sulfur[14] as shown in Scheme 3. Thiophene coordination in either the π-allylpalladium complex (**9**) or the σ-allylpalladium complex (**10**) would result in retardation of the π–σ–π allyl isomerization pathway. Alternatively, as reversible ring opening of the product oxazline is necessary for equilibration, the thiophene substituent may be inhibiting the rate of oxidative addition of (**4**). However, given the variety of substituents tolerated at that position, the latter seems unlikely.

Surprisingly, when the electron rich aryl iodide, *p*-methoxyiodobenzene, was used a mixture of products was obtained (entry 20). Oxazoline (**4ef**) was produced in 50% yield accompanied by 37% of the phenyl derivative (**4ea**). Presumably, this product was the result of aryl exchange between the aryl palladium and the triphenylphosphine ligand.[15]

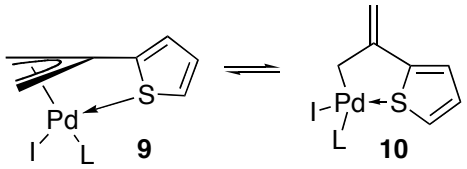
Table 3. Tandem arylation/oxazoline formation reaction scope



5 **4**

entry	substrate	ArI	product	yield %[a]	*trans:cis*[b]
1	**5a**	PhI	**4aa**	90	>99:1
2	**5a**	1-iodonaphthalene	**4ab**	85	>99:1
3	**5a**	2-iodothiophene	**4ac**	75	80:20
4	**5b**	PhI	**4ba**	70	>99:1
5	**5b**	1-iodonaphthalene	**4bb**	89	>99:1
6	**5b**	2-iodothiophene	**4bc**	72	75:25
7	**5c**	PhI	**4ca**	75	>99:1
8	**5c**	1-iodonaphthalene	**4cb**	93	>99:1
9	**5c**	2-iodothiophene	**4cc**	75	92:8
10	**5c**	*p*-MeC_6H_4I	**4cd**	76	>99:1
11	**5d**	PhI	**4da**	79	>99:1
12	**5d**	1-iodonaphthalene	**4db**	86	>99:1
13	**5d**	2-iodothiophene	**4dc**	57	63:37
14	**5d**	*p*-MeC_6H_4I	**4dd**	93	>99:1
15	**5d**	*m*-MeC_6H_4I	**4de**	62	>99:1
16	**5e**	PhI	**4ea**	95	>99:1
17	**5e**	1-iodonaphthalene	**4eb**	85	>99:1
18	**5e**	*p*-MeC_6H_4I	**4ed**	74	>99:1
19	**5e**	*m*-MeC_6H_4I	**4ee**	69	>99:1
20	**5e**	*p*-$MeOC_6H_4I$	**4ef**	50 (+ 37)[c]	>99:1

[a]Isolated yield. [b]Measured by ^1H NMR spectroscopy. [c]Compound (**4ea**) was also formed *via* aryl exchange with PPh_3.



Scheme 3. Possible thiophene coordination

In conclusion, we have demonstrated a highly selective preparation of chiral oxazolines *via* a tandem palladium-catalyzed arylation/cyclization strategy. This method allowed for the facile generation of a variety of highly functionalized compounds simply by varying the aryl coupling partner.

Thiophene-derived substrates displayed lower selectivity, suggesting that thiophene coordination in the intermediate π-allyl palladium complex may be involved.

EXPERIMENTAL

General Experimental: Thin layer chromatography (TLC) was performed on silica gel Whatman-60F glass plates, and components were visualized by illumination with UV light or by staining with potassium permanganate solution. Chromatography was performed using silica E. Merck silica gel 60 (230-400 mesh). NMR spectra were recorded in DMSO or $CDCl_3$ on a Varian Inova 500 MHz, 400 MHz, or Varian Mercury 300 MHz spectrometer. ^{13}C NMR spectra were recorded using broad band proton decoupling. Chemical shifts are reported in δ relative to TMS and coupling constants in Hz. Optical rotations were recorded on a JASCO-CIP-370 instrument. High-resolution mass (HRMS) spectra [Electrospray (ES)] were obtained at the Mass Spectrometry Laboratory in the Department of Chemistry and Molecular Biology at North Dakota State University. Melting points were determined without correction. Reactions were carried out under an inert atmosphere of nitrogen or argon. Solvents were dried using a nitrogen pressurized alumina column system from Solvtek and degassed prior to use.

General Procedure for the Synthesis of Alkynols (7). The ester (**6**) (25 mmol) was dissolved in dry THF (100 mL) and cooled to -78 °C. To this was added a solution of DIBAL-H (50 mmol, 1.5*M* in hexane) through an addition funnel dropwise at a rate to maintain the temperature at a constant -78 °C. The reaction was stirred at this temperature for 20 min after the addition was complete and then ethynylmagnesium bromide (75 mmol, 0.5*M* in THF) was added in the same manner. When the addition was complete, the flask was transferred to an ice bath and the reaction was allowed to slowly warm to rt overnight. The reaction was slowly quenced with saturated ammonium chloride solution at 0 °C. The aqueous layer was extracted with ether (3 x 100 mL). The combined organic extracts were washed with brine and dried with sodium sulfate. After filtration, the solvent was removed by rotary evaporation and the crude alkynol was purified by flash chromatograpy on silica gel (ethyl acetate:hexane, 1:1).

***N*-((2*S*)-3-Hydroxy-1-phenylpent-4-yn-2-yl)benzamide (7a)**. Mixture of *syn:anti* (70:30). ^1H NMR (300 MHz, $CDCl_3$) δ 7.69-7.63 (m, 2 H), 7.53-7.47 (m, 1 H), 7.43-7.38 (m, 2 H), 7.36-7.22 (m, 5 H), 6.44 (d, J = 8.1 Hz, 0.7 H), 6.31 (d, J = 8.0 Hz, 0.3 H), 4.60-4.52 (m, 1 H), 4.49-4.40 (m, 1 H), 3.21-2.97 (m, 2 H), 2.57 (d, J = 1.8 Hz, 0.3 H), 2.48 (d, J = 2.1 Hz, 0.6 H); ^{13}C NMR (25 MHz, $CDCl_3$) δ 168.6, 137.6, 134.4, 132.2, 132.0, 129.9, 129.5, 129.3, 129.1, 128.9, 127.3, 127.1, 75.4, 74.6, 65.7, 63.7, 56.6, 56.2, 37.2, 36.6. IR (neat) 3292, 3028, 2359, 2116, 1640, 1536, 1489, 1043, 701 cm^{-1}; MS (m/z) 302 (M+Na); HRMS calcd for $C_{18}H_{17}NO_2Na^+$ 302.1151, found 302.1153.

***N*-((3*S*)-4-Hydroxy-2-methylhex-5-yn-3-yl)benzamide (7b)**. Mixture of *syn:anti* (90:10). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.79 (m, 2 H), 7.53-7.44 (m, 1 H), 7.40 (d, *J* = 7.5 Hz, 2 H), 6.68 (d, *J* = 9.0 Hz, 0.9 H), 6.35 (d, *J* = 9.5 Hz, 0.1 H), 4.70 (br, 0.1 H), 4.63 (br, 0.9 H), 4.14 (dd, *J* = 9.0, 3.0 Hz. 0.1 H), 4.00 (ddd, *J* = 9.0, 4.0, 1.5 Hz, 0.9 H), 3.85-3.79 (br, 1 H), 2.50 (d, *J* = 2.5 Hz, 0.1 H), 2.39 (d, *J* = 2.0 Hz, 0.8 H), 2.24-2.14 (m, 0.9 H), 2.04-1.94 (m, 0.1 H), 1.05 (d, *J* = 7.0 Hz, 3 H), 1.01 (d, *J* = 2.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 134.7, 132.2, 131.8, 128.9, 128.8, 127.3, 83.3, 75.1, 74.1, 63.1, 60.5, 60.4, 30.5, 29.4, 20.2, 19.7, 19.2. IR (neat) 3404, 3300, 2963, 2359, 2114, 1635, 1539, 1489, 1047, 692 cm^{-1}; MS (m/z) 254 (M+Na); HRMS calcd for $C_{14}H_{17}NO_2Na^+$ 254.1151, found 254.1157.

***N*-((4*S*)-3-Hydroxy-6-methylhept-1-yn-4-yl)benzamide (7c)**. Mixture of *syn:anti* (70:30). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.75 (m, 2 H), 7.49-7.46 (m, 1 H), 7.39 (dd, *J* = 16.0, 9.0 Hz, 2 H), 6.49 (d, *J* = 9.0 Hz, 0.7 H), 6.42 (d, *J* = 8.5 Hz, 0.3 H), 4.55 (br, 0.3 H), 4.51 (br, 0.7 H), 4.45 (m, 0.3 H), 4.40-4.36 (m, 0.7 H), 4.26-4.25 (m, 0.3 H), 4.11-4.08 (m, 0.7 H), 2.48 (d, *J* = 2.0 Hz, 0.3 H), 2.42 (d, *J* = 2.0 Hz, 0.6 H), 1.73-1.54 (m, 3 H), 0.97-0.94 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 168.5, 134.5, 134.2, 132.1, 131.9, 128.8, 128.8, 127.4, 127.3, 82.9, 82.1, 74.8, 74.2, 66.5, 64.9, 53.3, 52.7, 39.7, 39.2, 25.2, 23.6, 23.5, 22.2, 21.3. IR (neat) 3409, 3304, 2956, 2357, 2116, 1968, 1637, 1538, 1489, 1056, 693 cm^{-1}; MS (m/z) 268 (M+Na); HRMS calcd for $C_{15}H_{19}NO_2Na^+$ 268.1308, found 268.1307.

***N*-((4*S*)-3-Hydroxy-5-methylhept-1-yn-4-yl)benzamide (7d)**. Mixture of *syn:anti* (70:30). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80-7.76 (m, 2 H), 7.54-7.34 (m, 3 H), 6.79 (d, *J* = 9.6 Hz, 0.7 H), 6.38 (d, *J* = 9.0 Hz, 0.3 H), 4.70-4.66 (br, 1 H), 4.24-4.00 (m, 2 H), 2.49 (d, *J* = 2.1 Hz, 0.2H), 2.35 (d, *J* = 2.1 Hz, 0.5 H), 1.95-1.85 (m, 0.7 H), 1.74-1.68 (m, 0.3 H), 1.66-1.53 (m, 1 H), 1.30-1.10 (m, 1 H), 1.01 (t, *J* = 10.0 Hz, 3 H), 0.90 (dd, *J* = 23.0 and 10.0 Hz, 3 H); IR (neat) 3415, 3304, 2963, 2120, 1637, 1541, 1479, 1343, 1293, 1048, 691 cm^{-1}; MS (m/z) 268 (M+Na); HRMS calcd for $C_{15}H_{19}NO_2Na^+$ 268.1308, found 268.1306.

***N*-((2*S*)-3-Hydroxypent-4-yn-2-yl)benzamide (7e)**. Mixture of *syn:anti* (80:20). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79-7.76 (m, 2 H), 7.53-7.49 (m, 1 H), 7.45-7.41 (m, 2 H), 6.37 (br, 1 H), 4.56-4.52 (m, 1 H), 4.50-4.44 (m, 0.2 H), 4.43-4.36 (m, 0.8 H), 3.91-3.85 (br, 0.2H), 3.45-3.37 (br, 0.8 H), 2.51 (d, *J* = 2.0 Hz, 0.2 H), 2.47 (d, *J* = 2.0 Hz, 0.7 H), 1.38 (dd, *J* = 13.0 and 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 168.2, 159.5, 159.4, 134.4, 132.1, 131.9, 128.8, 127.3, 127.3, 82.5, 74.8, 74.4, 66.8, 65.7, 60.6, 50.8, 50.2, 21.3, 16.3, 16.1, 14.4. IR (neat) 3419, 2360, 2116, 1635, 1596, 1539, 1488, 1046 cm^{-1}; MS (m/z) 226 (M+Na); HRMS calcd for $C_{12}H_{13}NO_2Na^+$ 226.0838, found 226.0843.

General Procedure for the Synthesis of Acetates (8). The alcohol (**7**) (20 mmol) and DMAP (1.2 g, 10 mmol) were dissolved in Et_3N (20.2 g, 200 mmol). Acetic anhydride (10.2 g, 100 mmol) was added and the reaction was stirred at rt for several hours until complete as indicated by TLC. Water was added and the product was extracted with dichloromethane (3 x 100 mL). The combined organic extracts were washed with brine and dried with anhydrous sodium sulfate. After filtration, the solvent was removed by rotary evaporation and the acetate was purified by flash chromatography on silica gel (ethyl acetate:hexane, 1:3).

(2*S*)-2-Benzamido-1-phenylpent-4-yn-3-yl acetate (8a). Mixture of *syn:anti* (70:30). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72-7.66 (m, 2 H), 7.50-7.47 (m, 1 H), 7.43-7.38 (m, 2 H), 7.32-7.29 (m, 3 H), 7.26-7.22 (m, 2 H), 6.40 (d, *J* = 9.0 Hz, 0.3 H), 6.33 (d, *J* = 9.0 Hz, 0.7 H), 5.50-5.47 (m, 1 H), 4.81-4.77 (m, 1 H), 3.13-3.03 (m, 2 H), 2.67 (d, *J* = 2.0 Hz, 0.3H), 2.54 (d, *J* = 2.0 Hz, 0.7 H), 2.09 (d, *J* = 24.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 169.8, 167.6, 167.5, 136.8, 136.7, 134.7, 134.5, 131.9, 131.8, 129.5, 129.3, 128.9, 128.8, 128.7, 127.3, 127.2, 127.1, 78.9, 78.2, 76.6, 75.7, 65.5, 64.7, 53.1, 52.6, 37.6, 36.8, 31.8, 22.9, 21.0, 14.4. IR (neat) 3427, 2360, 2124, 1645, 1231, 1033 cm^{-1}; MS (m/z) 344 (M+Na); HRMS calcd for $C_{20}H_{19}NO_3Na^+$ 344.1257, found 344.1256.

(4*S*)-4-Benzamido-5-methylhex-1-yn-3-yl acetate (8b). Mixture of *syn:anti* (80:20). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77-7.73 (m, 2 H), 7.48-7.44 (m, 1 H), 7.42-7.37 (m, 2 H), 6.32 (d, *J* = 10.0 Hz, 1 H), 5.65 (dd, *J* = 3.5, 2.0 Hz, 0.2 H), 5.60 (dd, *J* = 6.0, 2.0 Hz, 0.8 H), 4.39-4.34 (m, 0.8 H), 4.28-4.24 (m, 0.2 H), 2.58 (d, *J* = 2.5 Hz, 0.2 H), 2.45 (d, *J* = 2.0 Hz, 0.7 H), 2.03 (s, 3 H), 1.99 (dd, *J* = 6.5, 2.0 Hz, 1 H), 0.98 (d, *J* = 3.5 Hz, 3 H), 0.97 (d, *J* = 3.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 169.9, 167.9, 134.9, 134.8, 131.8, 128.8, 127.2, 79.1, 78.2, 77.6, 75.2, 65.1, 64.5, 60.6, 57.4, 56.6, 30.5, 29.7, 21.2, 20.9, 20.1, 19.8, 19.4, 18.2, 14.4. IR (neat) 3398, 2964, 2318, 2128, 1742, 1644, 1537, 1490, 1371, 1231, 1028, 693 cm^{-1}; MS (m/z) 296 (M+Na); HRMS calcd for $C_{16}H_{19}NO_3Na^+$ 296.1257, found 296.1251.

(4*S*)-4-Benzamido-6-methylhept-1-yn-3-yl acetate (8c). Mixture of *syn:anti* (70:30). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76-7.73 (m, 2 H), 7.49-7.45 (m, 1 H), 7.42-7.38 (m, 2 H), 6.24 (d, *J* = 9.5 Hz, 1 H), 5.48 (dd, *J* = 5.0, 2.0 Hz, 1 H), 4.64-4.54 (m, 1 H), 2.57 (d, *J* = 2.0 Hz, 0.3 H), 2.46 (d, *J* = 2.0 Hz, 0.7 H), 2.05 (d, *J* = 15.0 Hz, 3 H), 1.72-1.67 (m, 1 H), 1.59-1.49 (m, 2 H), 0.95 (dd, *J* = 6.5, 2.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 169.8, 167.6, 167.5, 134.7, 134.6, 131.8, 128.8, 127.2, 79.0, 78.4, 75.9, 75.2, 66.8, 65.7, 50.2, 49.7, 40.2, 39.7, 25.1, 25.0, 23.6, 23.3, 22.3, 22.0, 21.0. IR (neat) 3297, 2958, 2361, 2120, 1739, 1641, 1538, 1490, 1370, 1231, 1027, 694 cm^{-1}; MS (m/z) 310 (M+Na); HRMS calcd for $C_{17}H_{21}NO_3Na^+$ 310.1414, found 310.1410.

(4*S*)-4-Benzamido-5-methylhept-1-yn-3-yl acetate (8d). Mixture of *syn:anti* (90:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71-7.68 (m, 2 H), 7.42-7.37 (m, 1 H), 7.34-7.30 (m, 2 H), 6.43 (d, *J* = 10.4 Hz, 1 H), 5.62 (dd, *J* = 3.6, 2.4 Hz, 0.1 H), 5.57 (dd, *J* = 5.2, 2.4 Hz, 0.9 H), 4.35 (dd, *J* = 5.2, 2.4 Hz, 1 H), 2.56 (d, *J* = 2.4 Hz, 0.1 H), 2.40 (d, *J* = 2.4 Hz, 0.9 H), 1.97 (s, 3 H), 1.75-1.70 (m, 1 H), 1.56-1.47 (m. 1 H), 1.16-1.09 (m, 1 H), 0.89 (d, *J* = 6.8 Hz, 3 H), 0.83 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 167.9, 134.8, 134.7, 131.7, 128.7, 128.5, 127.2, 127.1, 79.2, 78.1, 75.2, 64.4, 36.1, 24.9, 20.9, 16.1, 11.5. IR (neat) 3396, 2970, 2132, 1742, 1643, 1537, 1483, 1363, 1230, 1026, 693 cm^{-1}; MS (m/z) 310 (M+Na); HRMS calcd for $C_{17}H_{21}NO_3Na^+$ 310.1414, found 310.1417.

(4*S*)-4-Benzamidopent-1-yn-3-yl acetate (8e). Mixture of *syn:anti* (70:30). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.70 (m, 2 H), 7.44-7.41 (m, 1 H), 7.37-7.33 (m, 2 H), 6.59 (d, *J* = 9.0 Hz, 1 H), 5.47-5.44 (m, 1 H), 4.57-4.47 (m, 1 H), 2.57 (d, *J* = 2.0 Hz, 0.3 H), 2.48 (d, *J* = 2.0 Hz, 0.7 H), 2.02 (d, *J* = 6.0 Hz, 3 H), 1.30 (t, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.7, 171.6, 170.2, 170.0, 167.7, 167.6, 134.4, 134.3, 131.9, 131.8, 127.3, 78.7, 78.3, 75.9, 75.5, 66.8, 65.9, 47.8, 47.7, 21.2, 21.0, 16.4, 16.2, 14.3. IR (neat) 3291, 2985, 2357, 2120, 1972, 1739, 1644, 1539, 1231, 1029, 694 cm^{-1}; MS (m/z) 268 (M+Na); HRMS calcd for $C_{14}H_{15}NO_3Na^+$ 268.0944, found 268.0944.

General Procedure A for the Synthesis of Allenes (5). PPh_3 (58 mg, 0.22 mmol) was placed into a dry Schlenk flask and degassed toluene (2.2 mL) was added. To this solution was added NaOBu-*t* (11 mg, 0.11 mmol) and CuCl (11 mg, 0.11 mmol) and the resulting solution was degassed again by the freeze pump thaw method and was stirred under argon for 10-20 min. Silane (Me_2PhSiH, 2.7 g, 20 mmol or PMHS, 0.5 mL) was added to the mixture resulting in a reddish orange solution. The acetate (**8**) (2 mmol) was added and the reaction was allowed to stir at rt overnight. The reaction flask was opened to air to decompose the excess copper hydride reagent. The mixture was filtered through a plug of silica gel and concentrated under reduced pressure. The crude allene (**5**) was purified by flash chromatography on silica gel (ethyl acetate:hexane, 1:5).

General Procedure B for the Synthesis of Allenes (5). The acetate (**8**) (2 mmol), CuF_2 (81 mg, 0.8 mmol), and PPh_3 (209 mg, 0.8 mmol) were dissolved in toluene (10 mL) and $PhSiH_3$ (519 mg, 4.8 mmol) was added. The reaction was allowed to stir at rt overnight. The mixture was filtered through a plug of silica gel and concentrated under vacuum to yield a crude oil. The allene (**5**) was purified by flash chromatography on silica gel (ethyl acetate:hexane, 1:5).

(*S*)-*N*-(1-Phenylpenta-3,4-dien-2-yl)benzamide (5a). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.70 (m, 2 H), 7.51-7.48 (m, 1 H), 7.43-7.38 (m, 2 H), 7.35-7.30 (m, 3 H), 7.27-7.23 (m, 2 H), 6.18 (d, *J* = 7.5 Hz, 1 H), 5.35 (ddd, *J* = 11.5, 6.5, 1.5 Hz, 1 H), 4.99-4.96 (m, 1 H), 4.92-4.85 (m, 2 H), 3.08 (dd, *J* = 13.5, 5.5 Hz, 1 H), 3.00 (dd, *J* = 13.5, 7.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.1 166.9, 137.4, 134.9, 134.0, 133.9, 133.3, 131.7, 129.9, 129.8, 129.5, 128.9, 128.8, 128.7, 128.6, 128.1, 127.1, 126.9, 92.3, 79.2, 48.5, 41.3, 31.8, 22.9, 14.4. IR (neat) 3431, 2357, 2157, 1635, 1245, 1044 cm^{-1}; MS (m/z) 286 (M+Na); HRMS calcd for $C_{18}H_{17}NONa^+$ 286.1208, found 286.1203.

(*S*)-*N*-(2-Methylhexa-4,5-dien-3-yl)benzamide (5b). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.76 (m, 2 H), 7.51-7.48 (m, 1 H), 7.45-7.41 (m, 2 H), 6.19 (d, *J* = 7.5 Hz, 1 H), 5.30 (ddd, *J* = 12.5, 6.0, 1.0 Hz, 1 H), 4.90 (dd, *J* = 7.5, 3.5 Hz, 2 H), 4.63-4.59 (m, 1 H), 2.02 (ddd, *J* = 12.0, 5.5, 1.5 Hz, 1 H), 0.99 (d, *J* = 5.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.6 167.1, 135.2, 134.0, 133.9, 131.6, 128.9, 128.8, 127.1, 127.0, 91.1, 78.5, 52.6, 32.9, 18.6, 18.5. IR (neat) 3431, 2368, 2104, 1949, 1635, 1541, 694 cm^{-1}; MS (m/z) 238 (M+Na); HRMS calcd for $C_{14}H_{17}NONa^+$ 238.1202, found 238.1210.

(*S*)-*N*-(6-methylhepta-1,2-dien-4-yl)benzamide (5c). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.70 (m, 2 H), 7.50-7.45 (m, 1 H), 7.43-7.38 (m, 2 H), 5.99 (d, *J* = 8.4 Hz, 1 H), 5.32 (ddd, *J* = 12.0, 5.6, 1.2 Hz, 1 H), 4.86 (dd, *J* = 6.8, 3.6, 1.6 Hz, 2 H), 4.78-4.73 (m, 1 H), 1.77-1.66 (m, 1 H), 1.57-1.50 (m, 3 H), 0.95 (d, *J* = 2.4 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6 167.1, 135.2, 135.0, 131.6, 128.7, 127.0, 93.3, 78.5, 46.1, 44.8, 25.3, 22.9, 22.7. IR (neat) 3429, 2349, 2139, 1953, 1646, 1537, 1363, 1231, 1040, 842 cm^{-1}; MS (m/z) 252 (M+Na); HRMS calcd for $C_{15}H_{19}NONa^+$ 252.1359, found 252.1363.

***N*-((4*S*)-5-Methylhepta-1,2-dien-4-yl)benzamide (5d)**. Mixture of amide rotational isomers (55:45). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.73 (m, 2 H), 7.50-7.45 (m, 1 H), 7.43-7.38 (m, 2 H), 6.18 (d, *J* = 8.4 Hz, 0.45 H), 6.02 (d, *J* = 8.8 Hz, 0.55 H), 5.88-5.77 (m, 0.55 H), 5.71-5.62 (m, 0.45 H), 5.46-5.34 (m, 0.55 H), 5.13-5.05 (m, 1 H), 4.91-4.86 (m, 0.45 H), 4.58-4.53 (m, 0.45 H), 4.18-4.11 (m, 0.55 H), 2.44-2.37 (m, 0.45 H), 2.28-2.20 (m, 0.55 H), 1.75 (dd, *J* = 6.8, 1.6 Hz, 0.45 H), 1.69 (ddd, *J* = 6.4, 1.6, 0.4 Hz, 0.55 H), 1.67-1.61 (m, 1 H), 1.60-1.47 (m, 1 H), 1.23-1.09 (m, 1 H), 0.96-0.91 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 166.8, 135.3, 135.2, 134.4, 134.2, 133.8, 131.6, 131.5, 129.6, 129.2, 128.9, 128.7, 128.6, 128.4, 127.8, 127.1, 127.0, 119.8, 117.8, 115.7, 90.5, 78.4, 55.8, 53.3, 50.9, 39.5, 39.4, 39.2, 38.3, 36.1, 25.9, 25.6, 18.1, 15.5, 15.3, 15.0, 14.9, 13.9, 11.9, 11.8. IR (neat) 3341, 2962, 2349, 2139, 1953, 1632, 1536, 1490, 1133, 695 cm^{-1}; MS (m/z) 252 (M+Na); HRMS calcd for $C_{15}H_{19}NONa^+$ 252.1359, found 252.1360.

(*S*)-*N*-(Penta-3,4-dien-2-yl)benzamide (5e). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77-7.73 (m, 2 H), 7.50-7.47 (m, 1 H), 7.44-7.41 (m, 2 H), 6.19 (br, 1 H), 5.38 (ddd, *J* = 11.5, 6.5, 1.5 Hz, 0.7 H), 5.13 (d, *J* = 9.0 Hz, 0.3 H), 4.96-4.89 (m, 2 H), 4.81-4.76 (m, 1 H), 1.36 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.1, 166.9, 134.9, 134.5, 134.4, 133.7, 133.6, 131.5, 130.8, 128.8, 128.0, 127.1, 127.0, 94.2, 78.9, 45.2, 43.5, 41.1, 20.9, 20.5. IR (neat) 3297, 2974, 2349, 1957, 1631, 1530, 1491, 1126, 695 cm^{-1}; MS (m/z) 210 (M+Na); HRMS calcd for $C_{12}H_{13}NONa^+$ 210.0895, found 210.0905.

General Procedure for the Tandem Allene Arylation/Cyclization to Give Oxazolines (4). To a mixture of allene (**5**) (1 equiv.), aryl iodide (1.2 equiv.), potassium carbonate (4 equiv.) and TBAB (0.1 equiv.) in MeCN (0.2 *M*) was added $Pd(PPh_3)_4$ (0.05 equiv.) under an atmosphere of argon. The reaction was heated to reflux and allowed to react until complete as indicated by TLC. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (hexane/ethyl acetate = 20:1) to afford the oxazoline (**4**).

(4*S*,5*S*)-4-Benzyl-2-phenyl-5-(1-phenylvinyl)-4,5-dihydrooxazole (4aa). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.98 (m, 2 H), 7.73-7.67 (m, 1 H), 7.51-7.47 (m, 2 H), 7.45-7.40 (m, 3 H), 7.24-7.15 (m, 5 H), 7.12-7.01 (m, 2 H), 5.21-5.20 (m, 2 H), 5.17 (br, 1 H), 4.23 (ddd, *J* = 10.0, 7.5, 2.5 Hz, 1 H), 3.07 (dd, *J* = 17.0, 7.0 Hz, 1 H), 2.73 (dd, *J* = 17.0, 10.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.6, 129.8, 128.6, 128.5, 127.9, 127.2, 126.7, 113.7, 84.3, 73.4, 42.0. IR (neat) 2916, 2345, 1658, 1650, 1487, 1448, 1324, 1281, 694 cm^{-1}; $[\alpha]^{25}_D$ = +22.93° (c = 0.41, $CHCl_3$); MS (m/z) 340 (M+1); HRMS calcd for $C_{24}H_{21}NOH^+$ 340.1696, found 340.1695.

(4*S*,5*S*)-4-Benzyl-5-(1-(naphthalen-1-yl)vinyl)-2-phenyl-4,5-dihydrooxazole (4ab). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02-8.00 (m, 2 H), 7.86 (d, *J* = 8.0 Hz, 1 H), 7.81 (d, *J* = 7.5 Hz, 1 H), 7.73 (d, *J* = 8.5 Hz, 1 H), 7.53-7.43 (m, 5 H), 7.30 (d, *J* = 7.5 Hz, 1 H), 7.15 (d, *J* = 7.0 Hz, 1 H), 7.02-6.99 (m, 3 H), 6.86-6.84 (m, 2 H), 5.59 (s, 1 H), 5.19 (d, *J* = 6.0 Hz, 2 H), 4.33 (ddd, *J* = 11.5, 6.0, 2.5 Hz, 1 H), 2.94 (dd, *J* = 13.5, 5.5 Hz, 1 H), 2.54 (dd, *J* = 13.5, 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 145.9, 137.1, 135.9, 133.9, 131.9, 131.6, 129.4, 128.6, 128.5, 128.3, 128.0, 126.5, 126.4, 126.3, 125.9, 125.6, 125.3, 116.1, 85.4, 73.0, 42.1. IR (neat) 3059, 2345, 1957, 1817, 1650, 1494, 1321, 695 cm^{-1}; $[\alpha]^{25}_D$ = +4.48° (c = 1.25, $CHCl_3$); MS (m/z) 390 (M+1); HRMS calcd for $C_{28}H_{23}NOH^+$ 390.1852, found 390.1867.

(4*S*,5*S*)-4-Benzyl-2-phenyl-5-(1-(thiophen-2-yl)vinyl)-4,5-dihydrooxazole (4ac). Mixture of *trans:cis* (80:20). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.0, 1.5 Hz, 2 H), 7.52 (d, *J* = 7.0 Hz, 1 H), 7.45 (d,

J = 7.5 Hz, 2 H), 7.33-7.18 (m, 5 H), 7.16-7.09 (m, 1 H), 6.84 (dd, *J* = 5.0, 3.5 Hz, 1 H), 6.63 (d, *J* = 3.5 Hz, 1 H), 5.39 (s, 0.8 H), 5.24 (s, 0.2 H), 5.21 (s, 0.2 H), 5.15 (d, *J* = 6.5 Hz, 0.8 H), 5.05 (s, 1 H), 4.40 (ddd, *J* = 13.5, 6.0, 1.5 Hz, 0.8 H), 4.27 (ddd, *J* = 11.5, 6.0, 2.0 Hz, 0.2 H), 3.21 (dd, *J* = 12.0, 6.0 Hz, 0.8 H), 3.11 (dd, *J* = 14.0, 5.5 Hz, 0.2 H), 2.88 (dd, *J* = 13.5, 7.5 Hz, 0.8 H), 2.77 (dd, *J* = 13.5, 8.0 Hz, 0.2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4, 140.3, 140.2, 138.2, 137.6, 131.8, 131.7, 129.9, 129.8, 128.9, 128.7, 128.6, 128.5, 128.0, 127.8, 127.7, 127.2, 126.8, 126.7, 125.2, 124.6, 113.8, 113.2, 84.6, 84.3, 73.6, 73.4, 42.0. IR (neat) 3027, 2349, 1961, 1736, 1651, 1450, 1242, 1062, 695 cm^{-1}; MS (m/z) 346 (M+1); HRMS calcd for $C_{22}H_{19}NOSH^+$ 346.1260, found 346.1264.

(4*S*,5*S*)-4-Isopropyl-2-phenyl-5-(1-phenylvinyl)-4,5-dihydrooxazole (**4ba**). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.68 (m, 2 H), 7.23-7.20 (m, 1 H), 7.11-7.08 (m, 2 H), 7.04-6.95 (m, 5 H), 5.00 (d, *J* = 19.0 Hz, 2 H), 4.86 (d, *J* = 6.0 Hz, 1 H), 3.54 (t, *J* = 6.0 Hz, 1 H), 1.52-1.48 (m, 1 H), 0.56 (dd, *J* = 7.0, 4.5 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 148.4, 140.0, 138.9, 133.2, 131.5, 129.5, 128.7, 128.6, 128.5, 128.2, 128.1, 127.9, 127.7. IR (neat) 2959, 2361, 1652, 1440, 1067, 693 cm^{-1}; $[\alpha]^{25}_D$ = +8.29° (c = 0.21, $CHCl_3$); MS (m/z) 292 (M+H); HRMS calcd for $C_{20}H_{21}NOH^+$ 292.1696, found 292.1697 .

(4*S*,5*S*)-4-Isopropyl-5-(1-(naphthalen-1-yl)vinyl)-2-phenyl-4,5-dihydrooxazole (**4bb**). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10-8.09 (m, 1 H), 8.01 (dd, *J* = 7.0 and 1.5 Hz, 2 H), 7.93-7.85 (m, 2 H), 7.81 (d, *J* = 8.0 Hz, 1 H), 7.62-7.57 (m, 1 H), 7.53-7.49 (m, 3 H), 7.45-7.42 (m, 3 H), 7.37 (dd, *J* = 7.0, 1.5 Hz, 1 H), 5.71 (s, 1 H), 5.28 (s, 1 H), 5.18 (d, *J* = 5.5 Hz, 1 H), 4.15 (s, 1 H), 3.93 (d, *J* = 5.5 Hz, 1 H), 1.68-1.64 (m, 2 H), 0.65 (dd, *J* = 10.0, 7.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 146.9, 136.5, 133.9, 132.1, 131.5, 129.4, 129.3, 128.6, 128.5, 128.4, 128.0, 127.3, 126.8, 126.7, 126.6, 126.5, 126.1, 125.7, 125.3, 122.6, 115.9, 83.6, 32.7, 21.9, 18.4, 17.9. IR (neat) 3064, 2958, 2349, 2252, 1656, 1650, 1449, 1340, 1063, 779 cm^{-1}; $[\alpha]^{25}_D$ = -62.96° (c = 0.14, $CHCl_3$); MS (m/z) 342 (M+1); HRMS calcd for $C_{24}H_{23}NOH^+$ 342.1852, found 342.1848.

(4*S*,5*S*)-4-Isopropyl-2-phenyl-5-(1-(thiophen-2-yl)vinyl)-4,5-dihydrooxazole (**4bc**). Mixture of *trans:cis* (75:25). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01-7.98 (m, 2 H), 7.50-7.45 (m, 1 H), 7.43-7.39 (m, 2 H), 7.19 (dd, *J* = 6.5, 1.5 Hz, 1 H), 7.03 (dd, *J* = 4.5, 1.5 Hz, 1 H), 6.94 (ddd, *J* = 6.5, 4.5, 1.0 Hz, 1 H), 5.50 (s, 0.75H), 5.33 (d, *J* = 1.5 Hz, 0.25 H), 5.29 (s, 0.25 H), 5.27 (s, 0.75 H), 5.16 (d, *J* = 3.0 Hz, 0.25 H), 5.08 (d, *J* = 3.5 Hz, 0.75 H), 3.99 (dd, *J* = 8.5, 2.0 Hz, 0.75 H), 3.85 (d, *J* = 2.5 Hz, 0.25 H), 1.99-1.87 (m, 0.75 H), 1.85-1.77 (m, 0.25 H), 0.98 (dd, *J* = 10.5, 2.0 Hz, 4.5 H), 0.86 (dd, *J* = 8.5, 5.0 Hz, 1.5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.5, 128.6, 128.5, 127.7, 127.6, 125.4, 124.9, 114.4, 84.3, 33.2,

32.9, 19.0, 18.6, 18.3, 18.2. IR (neat) 2959, 2349, 1646, 1444, 1060, 693 cm^{-1}; MS (m/z) 298 (M+1); HRMS calcd for $C_{18}H_{19}NSOH^+$ 298.1266, found 298.1267.

(4*S*,5*S*)-4-Isobutyl-2-phenyl-5-(1-phenylvinyl)-4,5-dihydrooxazole (4ca). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02-8.00 (m, 2 H), 7.51-7.48 (m, 1 H), 7.45-7.42 (m, 2 H), 7.38-7.30 (m, 5 H), 5.35 (d, *J* = 15.0 Hz, 2 H), 5.08 (d, *J* = 6.5 Hz, 1 H), 4.03 (dd, *J* = 14.0, 7.0 Hz, 1 H), 1.78 (dd, *J* = 13.5, 6.5 Hz, 1 H), 1.59 (dd, *J* = 14.0, 7.5 Hz, 1 H), 1.36 (dd, *J* = 13.5, 6.5 Hz, 1 H), 0.86 (d, *J* = 6.5 Hz, 3 H), 0.77 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 147.6, 138.8, 128.7, 128.6, 128.5, 128.2, 128.1, 127.6, 127.4, 114.2, 86.6, 70.8, 46.2, 25.1, 22.9, 22.7. IR (neat) 2955, 2353, 1957, 1650, 1580, 1449, 1323, 1061, 777, 694 cm^{-1}; $[\alpha]^{25}_D$ = -11.79° (c = 2.04, $CHCl_3$); MS (m/z) 306 (M+1); HRMS $C_{21}H_{23}NOH^+$ calcd for 306.1852, found 306.1877.

(4*S*,5*S*)-4-Isobutyl-5-(1-(naphthalen-1-yl)vinyl)-2-phenyl-4,5-dihydrooxazole (4cb). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 7.0, 2.5 Hz, 1 H), 8.01 (dd, *J* = 7.0, 1.5 Hz, 2 H), 7.86 (dd, *J* = 7.0, 2.0 Hz, 1 H), 7.82 (d, *J* = 8.0 Hz, 1 H), 7.53-7.48 (m, 3 H), 7.46-7.42 (m, 3 H), 7.38 (dd, *J* = 7.0, 1.0 Hz, 1 H), 5.74 (d, *J* = 1.5 Hz, 1 H), 5.29 (s, 1 H), 5.07 (d, *J* = 6.5 Hz, 1 H), 4.10 (dd, *J* = 13.5, 7.5 Hz, 1 H), 1.50-1.40 (m, 2 H), 1.07 (dd, *J* = 13.0, 1.5 Hz, 1 H), 0.69 (d, *J* = 6.5 Hz, 3 H), 0.55 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 146.2, 136.5, 133.9, 132.1, 131.5, 128.6, 128.5, 128.4, 128.2, 126.7, 126.5, 126.1, 125.7, 125.3, 115.9, 87.2, 70.3, 46.1, 24.9, 22.8, 22.5. IR (neat) 2954, 2349, 1957, 1650, 1580, 1449, 1319, 1061, 779, 694 cm^{-1}; $[\alpha]^{25}_D$ = -77.23° (c = 1.09, $CHCl_3$); MS (m/z) 356 (M+1); HRMS calcd for $C_{25}H_{25}NOH^+$ 356.2009, found 356.2016.

(4*S*,5*S*)-4-Isobutyl-2-phenyl-5-(1-(thiophen-2-yl)vinyl)-4,5-dihydrooxazole (4cc). Mixture of *trans:cis* (92:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-7.99 (m, 2 H), 7.51-7.47 (m, 1 H), 7.44-7.40 (m, 2 H), 7.21 (dd, *J* = 5.2, 1.2 Hz, 1 H), 7.06 (dd, *J* = 3.6, 1.2 Hz, 1 H), 6.97 (dd, *J* = 5.2, 3.6 Hz, 1 H), 5.52 (s, 0.92H), 5.36 (d, *J* = 1.2 Hz, 0.08 H), 5.08 (d, *J* = 6.8 Hz, 0.08 H), 4.98 (d, *J* = 6.8 Hz, 0.92 H), 4.18 (dd, *J* = 14.4, 6.4 Hz, 0.92 H), 4.03 (dd, *J* = 14.0, 2.8 Hz, 0.08 H), 1.92 (ddd, *J* = 20.4, 13.6, 2.8 Hz, 0.92 H), 1.77 (dd, *J* = 13.6, 2.8 Hz, 0.08 H), 1.68 (ddd, *J* = 13.6, 6.8, 1.2 Hz, 0.92 H), 1.59 (dd, *J* = 13.6, 3.6 Hz, 0.08 H), 1.50 (ddd, *J* = 13.6, 6.0, 0.8 Hz, 0.92 H), 1.35 (dd, *J* = 13.6, 6.8 Hz, 0.08 H), 0.94 (d, *J* = 6.4 Hz, 2.8 H), 0.90 (d, *J* = 6.8 Hz, 2.8 H), 0.85 (d, *J* = 6.8 Hz, 0.2 H), 0.76 (d, *J* = 6.8 Hz, 0.2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 140.6, 131.6, 128.7, 128.6, 128.5, 128.0, 127.6, 125.5, 124.8, 114.2, 113.9, 87.2, 70.7, 46.2, 25.2, 25.1, 23.1, 22.9. IR (neat) 2954, 2349, 1656, 1448, 1060, 693 cm^{-1}; MS (m/z) 312 (M+1); HRMS calcd for $C_{19}H_{21}NOSH^+$ 312.1422, found 312.1428.

(4*S*,5*S*)-Isobutyl-2-phenyl-5-(1-*p*-tolylvinyl)-4,5-dihydrooxazole (4cd). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 7.5, 1.0 Hz, 2 H), 7.52-7.49 (m, 1 H), 7.44 (d, *J* = 7.5 Hz, 2 H), 7.38-7.33 (m, 2 H), 7.28 (d, *J* = 7.5 Hz, 1 H), 7.15 (d, *J* = 8.0 Hz, 1 H), 5.38 (d, *J* = 17.0 Hz, 1 H), 5.34 (d, *J* = 5.5 Hz, 1 H), 5.09 (d, *J* = 7.0 Hz, 1 H), 4.06 (dd, *J* = 14.0, 7.0 Hz, 1 H), 2.36 (s, 3 H), 1.83 (dd, *J* = 13.5, 7.0 Hz, 1 H), 1.62 (dd, *J* = 13.5 and 7.0 Hz, 1 H), 1.39 (dd, *J* = 13.5, 7.0 Hz, 1 H), 0.89 (d, *J* = 6.5 Hz, 3 H), 0.81 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 147.7, 147.4, 138.8, 138.0, 135.8, 131.5, 131.5, 129.7, 129.6, 129.4, 128.7, 128.6, 128.5, 128.2, 127.6, 127.4, 114.2, 113.6, 86.8, 86.7, 70.8, 46.3, 25.1, 22.9, 22.8, 22.7, 21.4. IR (neat) 2954, 2345, 1650, 1449, 1323, 1061, 694 cm^{-1}; $[\alpha]^{25}_D$ = -1.65° (c = 2.37, $CHCl_3$); MS (m/z) 320 (M+1); HRMS calcd for $C_{22}H_{25}NOH^+$ 320.2009, found 320.2000.

(4*S*,5*S*)-4-((*S*)-*sec*-Butyl)-2-phenyl-5-(1-phenylvinyl)-4,5-dihydrooxazole (4da). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02-7.98 (m, 2 H), 7.51-7.47 (m, 1 H), 7.44-7.40 (m, 2 H), 7.36-7.27 (m, 5 H), 5.32 (d, *J* = 21.0 Hz, 2 H), 5.19 (d, *J* = 6.5 Hz, 1 H), 3.99 (dd, *J* = 6.0, 2.5 Hz, 1 H), 1.68-1.64 (m, 1 H), 1.39-1.32 (m, 1 H), 1.14-1.08 (m, 1 H), 0.84 (dd, *J* = 7.0, 2.0 Hz, 3 H), 0.78 (dd, *J* = 7.5, 2.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 148.5, 138.9, 131.5, 128.7, 128.6, 128.5, 128.2, 128.0, 127.8, 126.9, 114.7, 82.9, 76.5, 39.5, 25.7, 14.8, 11.9. IR (neat) 2966, 2345, 1650, 1452, 1328, 1067, 780, 693 cm^{-1}; $[\alpha]^{25}_D$ = -8.89° (c = 0.32, $CHCl_3$); MS (m/z) 306 (M+1); HRMS calcd for $C_{21}H_{23}NOH^+$ 306.1852, found 306.1857.

(4*S*,5*S*)-4-((*S*)-*sec*-Butyl)-5-(1-(naphthalen-1-yl)vinyl)-2-phenyl-4,5-dihydrooxazole (4db). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.5 Hz, 1 H), 8.01 (dd, *J* = 7.0, 1.5 Hz, 2 H), 7.85 (dd, *J* = 7.0, 2.0 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.53-7.47 (m, 3 H), 7.45-7.41 (m, 3 H), 7.36 (dd, *J* = 7.0, 2.0 Hz, 1 H), 5.70 (s, 1 H), 5.27 (s, 1 H), 5.18 (d, *J* = 5.0 Hz, 1 H), 4.03 (d, *J* = 5.0 Hz, 1 H), 1.51-1.48 (m, 1 H), 1.09-1.04 (m, 1 H), 0.89-0.83 (m, 1 H), 0.62 (d, *J* = 6.5 Hz, 3 H), 0.59 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 133.9, 132.1, 131.5, 128.6, 128.5, 128.4, 126.8, 126.5, 126.1, 125.7, 125.3, 115.9, 83.2, 76.1, 39.3, 25.6, 14.2, 11.7. IR (neat) 2961, 2353, 1656, 1450, 1316, 1062, 779 cm^{-1}; MS (m/z) 356 (M+1); HRMS calcd for $C_{25}H_{25}NOH^+$ 356.2009, found 356.2004.

(4*S*,5*S*)-4-((*S*)-*sec*-Butyl)-2-phenyl-5-(1-(thiophen-2-yl)vinyl)-4,5-dihydrooxazole (4dc). Mixture of *trans:cis* (63:37). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 6.5, 1.5 Hz, 2 H), 7.50-7.46 (m, 1 H), 7.43-7.39 (m, 2 H), 7.18 (dd, *J* = 6.5, 1.5 Hz, 1 H), 7.03 (dd, *J* = 4.5, 1.0 Hz, 1 H), 6.94 (dd, *J* = 6.5, 4.5 Hz, 1 H), 5.50 (s, 0.63H), 5.33 (s, 0.37 H), 5.28 (d, *J* = 3.0 Hz, 1 H), 5.17 (d, *J* = 8.0 Hz, 0.37 H), 5.09 (d, *J* = 8.5 Hz, 0.63 H), 4.11 (dd, *J* = 8.5, 2.0 Hz, 0.63 H), 3.97 (d, *J* = 7.0 Hz, 0.37 H), 1.79-1.73 (m, 0.63 H), 1.66-1.62 (m, 0.37 H), 1.56-1.49 (m, 0.63 H), 1.38-1.31 (m, 0.37 H), 1.25-1.16 (m, 0.63 H), 1.14-1.06 (m, 0.37 H), 0.93-0.74 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.5, 128.6, 128.5, 128.1, 127.8, 127.6,

125.5, 124.9, 114.9, 83.8, 82.8, 76.4, 39.7, 25.7, 25.6, 15.1, 14.8, 11.8. IR (neat) 2959, 2353, 1658, 695 cm^{-1}; MS (m/z) 312 (M+1); HRMS calcd for $C_{19}H_{21}NOSH^+$ 312.1417, found 312.1425.

(4*S*,5*S*)-4-((*S*)-*sec*-Butyl)-2-phenyl-5-(1-*p*-tolylvinyl)-4,5-dihydrooxazole (4dd). ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 7.0, 1.5 Hz, 2 H), 7.51-7.48 (m, 1 H), 7.44-7.41 (m, 2 H), 7.36-7.29 (m, 2 H), 7.25 (d, *J* = 5.0 Hz, 1 H), 7.12 (d, *J* = 8.0 Hz, 1 H), 5.35-5.28 (m, 2 H), 5.18 (d, *J* = 7.0 Hz, 1 H), 3.98 (dd, *J* = 11.0, 5.0 Hz, 1 H), 2.33 (s, 3 H), 1.68-1.63 (m, 1 H), 1.41-1.34 (m, 1 H), 1.15-1.09 (m, 1 H), 0.84 (dd, *J* = 7.0, 3.5 Hz, 3 H), 0.79 (dd, *J* = 13.5, 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.9, 148.5, 148.3, 131.5, 129.3, 128.7, 128.6, 128.5, 128.2, 127.8, 127.6, 114.7, 114.2, 83.0, 82.9, 76.5, 39.5, 39.4, 25.7, 21.3, 14.9, 11.9. IR (neat) 2961, 2349, 1655, 1444, 1062, 693 cm^{-1}; $[\alpha]^{25}_D$ = -23.75° (c = 0.16, $CHCl_3$); MS (m/z) 320 (M+1); HRMS calcd for $C_{22}H_{25}NOH^+$ 320.2009, found 320.2026.

(4*S*,5*S*)-4-((*S*)-*sec*-Butyl)-2-phenyl-5-(1-*m*-tolylvinyl)-4,5-dihydrooxazole (4de). ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.0, 1.0 Hz, 2 H), 7.49 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.43 (d, *J* = 7.5 Hz, 2 H), 7.36-7.29 (m, 1 H), 7.20 (d, *J* = 7.5 Hz, 1 H), 7.15 (d, *J* = 7.0 Hz, 1 H), 7.10 (d, *J* = 7.5 Hz, 1 H), 5.35-5.28 (m, 2 H), 5.18 (d, *J* = 5.5 Hz, 1 H), 3.98 (dd, *J* = 10.0, 5.0 Hz, 1 H), 2.31 (s, 3 H), 1.67-1.64 (m, 1 H), 1.39-1.36 (m, 1 H), 1.13-1.11 (m, 1 H), 0.84 (d, *J* = 7.0 Hz, 3 H), 0.78 (dd, *J* = 7.5, 2.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 148.6, 138.8, 138.2, 131.5, 128.9, 128.7, 128.6, 128.5, 128.2, 127.8, 124.8, 114.7, 114.4, 82.8, 76.5, 39.5, 25.7, 21.6, 14.8, 11.9. IR (neat) 2959, 2345, 1650, 1452, 1067, 693 cm^{-1}; $[\alpha]^{25}_D$ = -6.00° (c = 0.03, $CHCl_3$); MS (m/z) 320 (M+1); HRMS calcd for $C_{22}H_{25}NOH^+$ 320.2009, found 320.2004.

(4*S*,5*S*)-4-Methyl-2-phenyl-5-(1-phenylvinyl)-4,5-dihydrooxazole (4ea). ^1H NMR (500 MHz, $CDCl_3$) δ 8.05-8.03 (m, 2 H), 7.52-7.49 (m, 1 H), 7.46-7.43 (m, 2 H), 7.41-7.32 (m, 5 H), 5.39 (dd, *J* = 7.5, 1.0 Hz, 2 H), 5.12 (dd, *J* = 7.0, 0.5 Hz, 1 H), 4.07 (dd, *J* = 13.5, 7.0 Hz, 1 H), 1.34 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8, 147.0, 138.5, 134.4, 131.6, 130.8, 129.6, 128.8, 128.6, 128.5, 128.3, 128.2, 128.0, 127.9, 127.3, 113.4, 87.4, 68.3, 22.2. IR (neat) 2967, 2349, 1965, 1650, 1580, 1449, 1324, 1059, 778, 694 cm^{-1}; $[\alpha]^{25}_D$ = +75.00° (c = 0.16, $CHCl_3$); MS (m/z) 264 (M+1); HRMS calcd for $C_{18}H_{17}NOH^+$ 264.1383, found 264.1391.

(4*S*,5*S*)-4-Methyl-5-(1-(naphthalen-1-yl)vinyl)-2-phenyl-4,5-dihydrooxazole (4eb). ^1H NMR (500 MHz, $CDCl_3$) δ 8.09-8.07 (m, 1 H), 8.00-7.98 (m, 2 H), 7.87-7.85 (m, 1 H), 7.82-7.80 (m, 1 H), 7.52-7.47 (m, 3 H), 7.46-7.40 (m, 3 H), 7.36 (dd, *J* = 7.0, 1.5 Hz, 1 H), 5.76 (d, *J* = 1.5 Hz, 1 H), 5.28 (s, 1 H), 5.02 (d, *J* = 7.0 Hz, 1 H), 4.11 (dd, *J* = 13.5, 6.5 Hz, 1 H), 1.10 (d, *J* = 1.5 Hz, 3 H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 162.7, 145.9, 136.5, 134.4, 133.9, 132.1, 131.6, 130.8, 128.6, 128.5, 128.4, 128.0, 127.9, 126.5, 126.2, 125.7, 125.4, 116.2, 88.7, 67.7, 22.1. IR (neat) 3426, 2916, 2345, 1650, 1440, 1332, 1110, 1060, 694 cm^{-1}; $[\alpha]^{25}_D$ = +43.80° (c = 0.50, $CHCl_3$); MS (m/z) 314 (M+1); HRMS calcd for $C_{22}H_{19}NOH^+$ 314.1539, found 314.1527.

(4*S*,5*S*)-4-Methyl-2-phenyl-5-(1-*p*-tolylvinyl)-4,5-dihydrooxazole (4ed). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.0, 1.5 Hz, 2 H), 7.52-7.48 (m, 1 H), 7.44 (dd, *J* = 8.0, 1.5 Hz, 2 H), 7.40-7.34 (m, 2 H), 7.29 (d, *J* = 8.0 Hz, 1 H), 7.16 (d, *J* = 8.5 Hz, 1 H), 5.39 (d, *J* = 7.0 Hz, 1 H), 5.35 (d, *J* = 1.5 Hz, 1 H), 5.11 (d, *J* = 7.0 Hz, 1 H), 4.05 (dd, *J* = 13.5, 7.0 Hz, 1 H), 2.36 (s, 3 H), 1.34 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8, 147.0, 146.8, 138.5, 138.1, 135.6, 131.6, 131.5, 129.8, 129.6, 129.5, 129.1, 128.9, 128.8, 128.6, 128.5, 128.3, 128.2, 128.1, 127.3, 127.1, 125.9, 113.4, 112.6, 87.4, 68.3, 67.3, 22.2, 22.1, 21.4. $[\alpha]^{25}_D$ = +2.48° (c = 0.69, $CHCl_3$); MS (m/z) 278 (M+1); HRMS calcd for $C_{19}H_{19}NOH^+$ 278.1539, found 278.1535.

(4*S*,5*S*)-4-Methyl-2-phenyl-5-(1-*m*-tolylvinyl)-4,5-dihydrooxazole (4ee). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.0, 1.5 Hz, 2 H), 7.52-7.49 (m, 1 H), 7.46 (d, *J* = 7.0 Hz, 2 H), 7.40-7.32 (m, 1 H), 7.25 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.20 (d, *J* = 8.0 Hz, 1 H), 7.14 (d, *J* = 7.5 Hz, 1 H), 5.39 (dd, *J* = 7.0, 1.0 Hz, 1 H), 5.36 (dd, *J* = 5.0, 1.0 Hz, 1 H), 5.11 (d, *J* = 7.0 Hz, 1 H), 4.05 (ddd, *J* = 13.5, 7.0, 1.5 Hz, 1 H), 2.36 (s, 3 H), 1.33 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8, 147.2, 147.0, 138.5, 138.4, 131.6, 130.6, 130.1, 129.6, 129.0, 128.9, 128.8, 128.6, 128.5, 128.3, 128.1, 128.0, 127.7, 127.3, 126.7, 126.5, 125.5, 124.3, 113.4, 113.0, 87.4, 87.3, 68.3, 22.2, 21.7. IR (neat) 2966, 2345, 1650, 1449, 1325, 1059, 694 cm^{-1}; $[\alpha]^{25}_D$ = +14.85° (c = 0.84, $CHCl_3$); MS (m/z) 278 (M+1); HRMS calcd for $C_{19}H_{19}NOH^+$ 278.1539, found 278.1536.

(4*S*,5*S*)-5-(1-(4-Methoxyphenyl)vinyl)-4-methyl-2-phenyl-4,5-dihydrooxazole (4ef). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 7.0, 2.0 Hz, 2 H), 7.50-7.49 (m, 1 H), 7.44 (d, *J* = 7.5 Hz, 2 H), 7.32 (dd, *J* = 7.0, 2.0 Hz, 2 H), 6.88 (dd, *J* = 7.0, 2.0 Hz, 2 H), 5.31 (s, 2 H), 5.07 (d, *J* = 6.5 Hz, 1 H), 4.04 (dd, *J* = 13.5, 7.0 Hz, 1 H), 3.82 (s, 3 H), 1.34 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 146.3, 131.6, 130.9, 128.9, 128.6, 128.5, 128.4, 128.1, 127.1, 114.2, 112.1, 87.6, 68.3, 55.5, 22.1. IR (neat) 2924, 2345, 1650, 1510, 1444, 1254, 1025, 695 cm^{-1}; $[\alpha]^{25}_D$ = +60.00° (c = 0.09, $CHCl_3$); MS (m/z) 294 (M+1); HRMS $C_{19}H_{19}NO_2H^+$ calcd for 294.1489, found 294.1489.

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