EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201700448

Link to VoR: http://dx.doi.org/10.1002/ejoc.201700448

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10.1002/ejoc.201700448

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Diastereoselective Synthesis of *trans*-2,3 Diaryl(heteroaryl) 3,6-Dihydropyrans by an Allylboration/Ring-Closing Metathesis Sequence

Pierre-Antoine Nocquet,[a] Andrei Corbu,[a] Lieven Meerpoel,[b] Ian Stansfield,[c] Didier Berthelot,[c] Patrick Angibaud[c] and Janine Cossy*[a]

Abstract: *trans*-2,3-Diaryl(heteroaryl) dihydropyrans were synthesized by an allylboration/ring-closing metathesis sequence, using allylboranes formed *in situ* from the corresponding allylic alcohol. Aryl(heteroaryl) substituents were thus installed diastereoselectively on dihydropyran rings in a *trans* fashion. These disubstituted dihydropyrans were further transformed into monosaccharide-like tetrahydropyrans.

Introduction

Functionalized dihydropyrans are important targets in organic synthesis as they can be transformed to a variety of natural products and/or bioactive compounds including glycals, pseudo-glycals, glycosides. As *C*-aryl glycosides have been recently reported to have important biological properties,[1] a number of synthetic methods have been developed to access these compounds, including cross-coupling reactions.[2] So far the arylation of glycals and glycosides has been restricted to monoarylation.[3] Very recently, vicinal diarylation of glycals and pseudo-glycals has been reported, leading to *cis*-diaryl glycals and pseudo-glycals.[4] These compounds can also be obtained by construction of the oxygen-containing 6-membered rings.[5] It is worth noting that mainly *cis*-2,3-diaryl derivatives have been obtained, the *trans*-isomers, with one or two heteroaryl substituents, have rarely been reported to our knowledge.[6]
As part of innovative efforts, pharmaceutical companies are constantly searching for novel building blocks. The presence of aryl and heteroaryl groups can have a huge influence on the bioactivity of molecules due to the binding affinities with the biological targets. Recently, 2-aryl(heteroaryl) glycosides have been reported to be useful kinase inhibitors.[7] In addition, 2,3-diaryl 3,6-dihydropyrans can be seen as surrogates of chromenes[8] and, as the presence of heteroaryl groups can reduce the lipophilicity and help creating binding interactions with biological targets, we embarked on the synthesis of *trans*-2,3-aryl(heteroaryl) DHPs of type **A1**, **A2** with one aryl and one heteroaryl substituent (Figure 1).

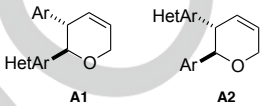
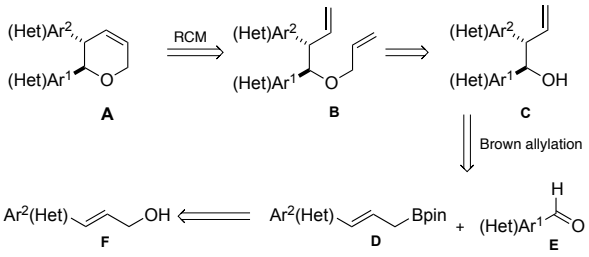


Figure 1. 2,3-Diarylated dihydropyrans **A1**, **A2**.

The synthetic strategy to access compounds of type **A** was based on a ring-closing metathesis applied to allyl ethers **B** to form the pyran ring (Scheme 1).[9] The homoallylic fragment bearing two vicinal aromatic/heteroaromatic substituents of these ethers **B** would come from homoallylic alcohols **C**. A allylboration was planned to access **C**, involving arylated allylic pinacol boronates **D** and various aryl(heteroaryl) aldehydes **E**.[10] It is worth noting that the reactivity of such complex boronates was seldom used in the synthesis of heteroaryl substrates.[11] The stereochemical outcome of the allylboration would depend on the configuration of the *in situ* generated allylboronates **D**. To access our targets, a palladium-catalyzed transformation of the corresponding allylic alcohols **F** would selectively grant *E*-allylic boronates **D**, that will inherently lead to the required homoallylic alcohol *anti* stereoisomers **C**.



Scheme 1. Retrosynthetic analysis of di-aryl(heteroaryl) DHPs.

Results and Discussion

For the synthesis of DHPs **A1**, arylated allylic alcohols **1a-d** were directly transformed into the corresponding pinacol-boronates using Szabó et al. and Kirschning et al. conditions.[12] These boronates were then converted to the *bis*-aryl(heteroaryl) homoallylic alcohols **3a-3f** by addition on various aromatic and heteroaromatic aldehydes. At first, the (3-phenylallyl)borane was prepared *in situ* by treatment of **1a** with the *bis*-pinacolborane [$(Bpin)_2$ (2.25 equiv)] in the presence of a palladium catalyst [$Pd(CH_3CN)_4(BF_4)_2$] in a mixture DMSO/MeOH (1:1) at 50 °C.

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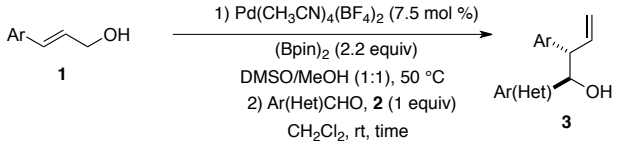
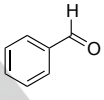
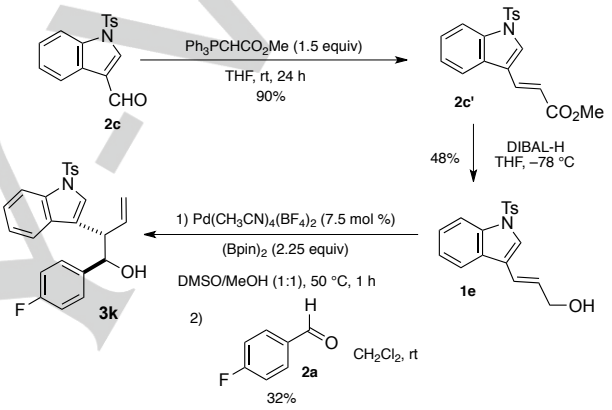
Table 1. Allylation of various (hetero)aromatic aldehydes using *in situ* generated allylboronates.



Entry	1	Ar(Het)CHO 2	time	3 (yield)
1	**1a**	**2a**	22 h	**3a** (99%)
2	**1a**	**2b**	46 h	**3b** (88%)
3	**1a**	**2c**	45 h	**3c** (97%)
4	**1a**	**2d**	94 h	**3d** (87%)
5	**1a**	**2e**	90 h	**3e** (97%)
6	**1a**	**2f**	22 h	**3f** (92%)
7	**1b**	**2f**	40 h	**3g** (61%)
8	**1c**	**2f**	40 h	**3h** (87%)
9	**1d**	**2f**	40 h	**3i** (53%)
10	**1c**		43 h	**3j** (93%)

After 2 h, the reaction mixture was worked-up and the aryl(heteroaryl) aldehydes **2a**-**f** were reacted with the crude pinacol boronates in CH_2Cl_2 to produce the desired homoallylic alcohols **3a**-**3f** in good yields (87-99%). The results are reported in Table 1. To access the homoallylic alcohols **3g**-**3j**, the allylic alcohols **1b**-**1d** were transformed to the corresponding boronates and further added to aldehyde **2f** and benzaldehyde to produce the corresponding homoallylic alcohols **3g**-**3j** in moderate to good yields (53%-93%). High diastereoselectivities were obtained (dr > 98:2) for **3a**-**3j** but at this stage the relative configuration of the two aryl(heteroaryl) groups could not be determined (cf *vide infra*).[13] The results are summarized in Table 1.

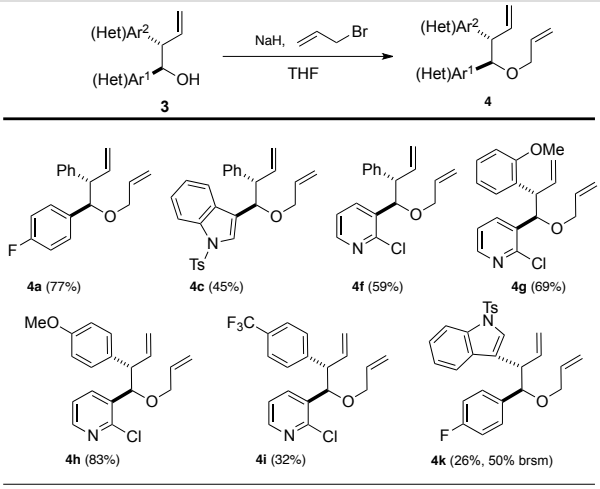
To access DHPs **A2** (Figure 1), allylic alcohol **1e** was prepared from *N*-tosyl β-indolylaldehyde by using a Wittig reaction and a DIBAL-H reduction. By applying the same conditions as reported in Table 1, homoallylic alcohol **3k**, bearing the heteroaryl at the C2-position, was obtained in a modest yield of 32% (Scheme 2).



Scheme 2. Synthesis 2-indolyl homoallylic alcohol **3k**.

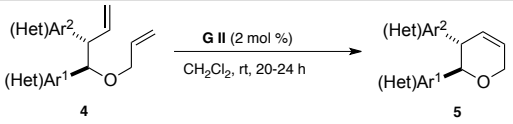
Having the homoallylic alcohols **3a**-**3k** in hand, their transformation to compounds **A** was examined. At first, the formation of the corresponding allylic ethers **B** was achieved *via* a conventional allylation using allylbromide under basic conditions (NaH, THF). The corresponding allylic ethers **4** were obtained in moderate to good yields (45%-83%), however, under these conditions **3b**, **3d** and **3e** could not be transformed to the corresponding allyl ethers **4** (Table 2).[14]

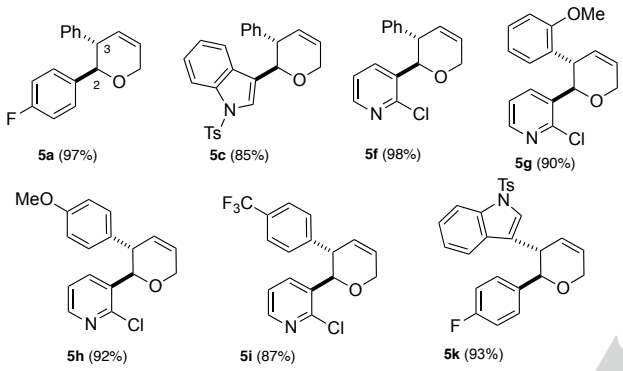
Table 2. Synthesis of Allyl-ethers **4**.



Compounds **4a**, **4c**, **4f**-**4i**, and **4k** were then involved in a ring-closing metathesis using the 2nd generation Grubbs catalyst (**GII**). The corresponding DHPs were isolated in good to excellent yields even for nitrogen containing heterocycles, as their inherent Lewis basicity was decreased by the presence of an adjacent chloride atom (**5f**-**5i**) (87-98%) or by the presence of a *N*-tosyl group (**5c**, 85%; **5k**, 93%).[15] The results are reported in Table 3.

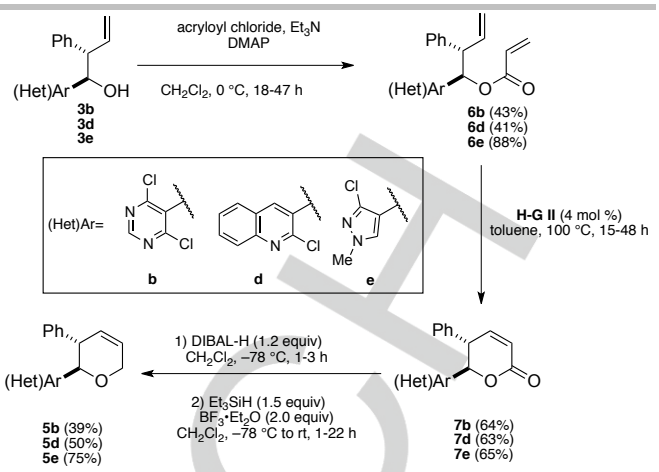
Table 3. Synthesis of 2,3 di(hetero)aryl substituted DHPs by RCM.





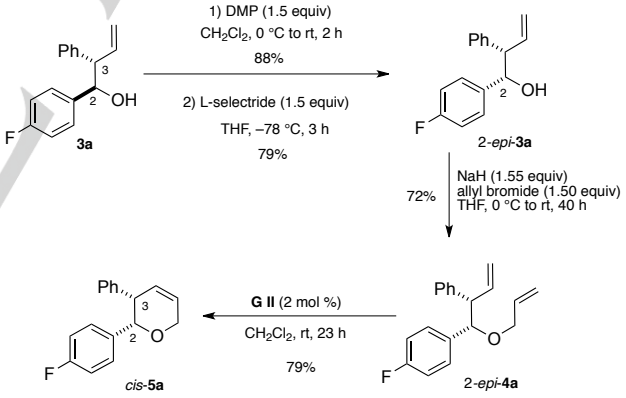
It is worth mentioning that the value of the coupling constant between H2 and H3 in compounds **5** is around 9 Hz, establishing the *trans* relationship between the aryl(heteroaryl) substituents on the DHP rings.

As ethers **4b**, **4d** and **4e** could not be obtained by the conventional allylation under basic conditions, an alternative route was devised, by synthesizing acrylates **6b**, **6d** and **6e** from homoallylic alcohols **3b**, **3d** and **3e** respectively (41%-88%) (Scheme 3). The pyranones **7b** (64%), **7d** (63%) and **7e** (65%) were then obtained by realizing a ring-closing metathesis using the 2nd generation Hoveyda-Grubbs catalyst (**H-GII**) in refluxing toluene. After reduction of the pyranones, using DIBAL-H to generate the intermediate lactols, followed by a Et_3SiH/BF_3•Et_2O reduction, the targeted DHPs **5b**, **5d** and **5e** were obtained (39%-75%).



Scheme 3. Alternative route towards **5b**, **5d**, **5e** DHPs, *via* a pyranone intermediate.

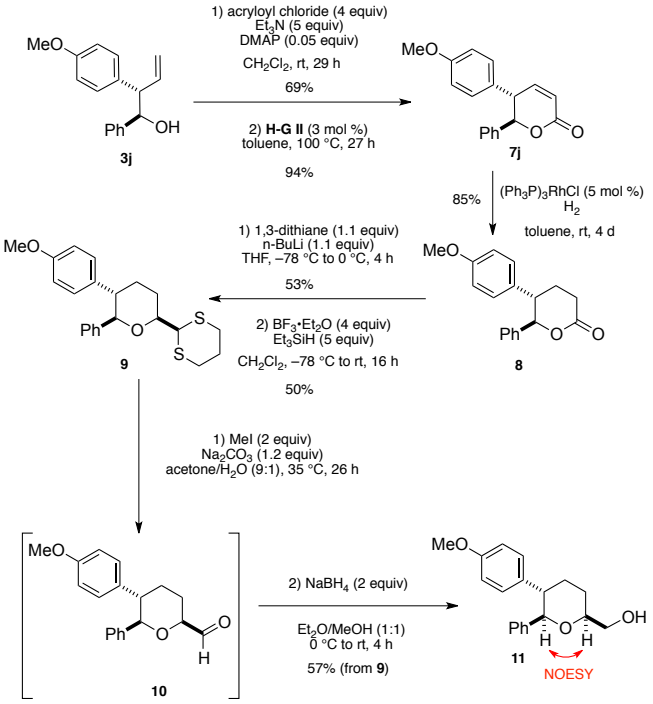
It is worth noting that the *anti*-isomers **3** can be transformed to their epimers at the C2 position, by an oxidation step (DMP, CH_2Cl_2, 0 °C to rt) followed by a reduction with L-selectride (THF -78 °C). Compound 2-*epi*-**3a** was obtained in a good overall yield as a single diastereomer (Scheme 4).[16] Allylation of 2-*epi*-**3a** generated 2-*epi*-**4a** in 72% yield, which was cyclized into the desired DHP *cis*-**5a** in 79% yield by using the 2nd generation Grubbs catalyst (**GII**). The *cis*-relative configuration was established by measuring the coupling constant between the protons H2 and H3 ($J_{H2,3}$=3.4 Hz) and by a NOESY experiment.



Scheme 4. Synthesis of *cis*-*bis*-arylated DHP *cis*-**5a** by an oxidation/reduction sequence.

As it was intended to reach glycoside-type compounds, further functionalization of the obtained DHPs was investigated. Thus, homoallylic alcohol **3j** was transformed to pyranone **7j**, using the previously described conditions (acylation, followed by a ring-closing metathesis, 65% over 2 steps). The reduction of the double bond present in **7j** was effected using the Wilkinson catalyst, generating lactone **8** (85%) that was treated with the lithiated 1,3-dithiane (53% yield) and the intermediate lactol was reduced using Et_3SiH/BF_3•Et_2O, to produce the homologated DHP **9** (50%).[17] Dithiane **9** was deprotected using MeI under basic conditions and the intermediate aldehyde **10** was reduced *in situ* by $NaBH_4$ to the 2,3-diaryl tetradeoxy carbohydrate **11** (57%, over the 2 steps) (Scheme 5). The *cis*-relative configuration of the phenyl and hydroxymethyl substituents at

C2 and C6 was respectively proven by a NOESY correlation of the protons H2 and H6.



Scheme 5. Synthesis of complex tetrahydropyrans, as glucoside analogs.

Conclusions

In summary, we have shown that *trans*-2,3-diarylated(heteroarylated) DHPs can be synthesized from aromatic and heteroaromatic aldehydes by using an allylboration followed by a ring-closing metathesis. The compatibility of the Hoveyda-Grubbs catalysts with the complex nitrogen-based heterocycles is assured by lowering the Lewis basicity of the nitrogen atom with electron-withdrawing groups. This versatile strategy provides an opportunity to obtain various original structures and substitution patterns on pyran rings in a diastereoselective manner. Further functionalization of the obtained DHPs and dihydropyranones can afford *C*-diaryl(heteroaryl) tetradeoxy-glycosides.

Experimental Section

General procedure 1 (GP1). *Synthesis of homoallylic alcohols **3**.* Allyl alcohol **1** (1.2 equiv) was added to a solution of $Pd(CH_3CN)_4(BF_4)_2$ (10 mol %) and $(Bpin)_2$ (2.5 equiv) in DMSO/MeOH (1:1, 0.25M). The solution was heated at 50 °C under air. After complete consumption of the starting material (1-5 h), the solution was cooled at rt and filtered through a pad of Celite and washed with Et_2O. The filtrate was concentrated under reduced pressure. Water was added and the product was extracted with Et_2O (3 times). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude boronate was diluted in CH_2Cl_2 (0.16 M) and aldehyde **2** (1 equiv) was added. The solution was stirred at rt, and after 22-90 h, H_2O was then added to the reaction mixture and the solution was stirred at rt for 1 h. The product was extracted with CH_2Cl_2 (3 times). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE) to afford homoallylic alcohol **3**.

General procedure 2 (GP2). *Synthesis of esters **6***

Acryloyl chloride (4 equiv) was added to a solution of alcohol **3** (1 equiv), Et_3N (5 equiv) and DMAP (0.1 equiv) in CH_2Cl_2 (0.12M) cooled at 0 °C. The solution was allowed to warm up to rt and stirred until complete consumption of starting material (18-48 h). A saturated aqueous solution of $NaHCO_3$ was then added and the product was extracted with CH_2Cl_2 (3 times). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE) to afford ester **6**.

(1*R,2*S**)-1-(4-fluorophenyl)-2-phenylbut-3-en-1-ol (3a).**

Compound **3a** was prepared according to **GP1** from cinnamyl alcohol (0.15 mL, 1.19 mmol) and *p*-fluorobenzaldehyde (86 µL, 0.795 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:6 to 1:5) to afford homoallylic alcohol **3a** (190 mg, 99%) as a slightly yellow oil. $\mathbf{R_f}$ = 0.31 (EtOAc/PE = 1:6); **IR** (film) 3428, 1603, 1509, 1220, 1156, 1032, 919 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.11 (m, 3H), 7.09 – 7.05 (m, 2H), 7.02 – 7.00 (m, 2H), 6.90 – 6.82 (m, 2H), 6.22 (ddd, *J* = 17.1, 10.2, 9.0 Hz, 1H), 5.28 – 5.21 (m, 2H), 4.78 (d, *J* = 8.0 Hz, 1H), 3.46 (t^{app}, *J* = 8.5 Hz, 1H), 1.9 (br s, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.9 (d, *J* = 245.2 Hz), 140.3, 137.7, 137.5 (d, *J* = 3.2 Hz), 128.3 (2C), 128.2 (d, *J* = 8.0 Hz, 2C), 128.1 (2C), 126.7, 118.7, 114.7 (d, *J* = 21.4 Hz, 2C), 76.65, 59.65; **EI–MS** *m/z* (relative intensity) 125 (99), 118 (100), 117 (54), 115 (34), 97 (63), 95(20), 91 (19), 77 (27); **HRMS** the compound was not detected.

(1*R,2*S**)-1-(4,6-Dichloropyrimidin-5-yl)-2-phenylbut-3-en-1-ol (3b).**

Compound **3b** was prepared according to **GP1** from cinnamyl alcohol (0.13 mL, 0.983 mmol) and 4,6-dichloropyrimidine-5-carbaldehyde (116 mg, 0.655 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:4 to 1:3) to afford homoallylic alcohol **3b** (171 mg, 88%) as a white solid. **mp** 91–92 °C; $\mathbf{R_f}$ = 0.36 (EtOAc/PE = 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.20 – 7.09 (m, 5H), 6.31 (m, 1H), 5.53 (dd, *J* = 10.2, 6.4 Hz, 1H), 5.41 (dt^{app}, *J* = 6.2, 0.9 Hz, 1H), 5.38 (d^{app}, *J* = 0.9 Hz, 1H), 4.27 (dd, *J* = 9.9, 8.4 Hz, 1H), 2.73 (d, *J* = 6.4 Hz, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.4 (2C), 156.3, 138.4, 137.3, 131.4, 128.7 (2C), 127.7 (2C), 127.5, 119.3, 72.8, 54.2; **IR** (film) 3397, 1532, 1515, 1415, 1334, 1214, 1130, 1048, 922, 854 cm^{-1}; **EI–MS** *m/z* (relative intensity) 175 (18), 118 (22), 117 (10) 116 (24), 115 (53), 91 (18), 86 (29), 85 (23), 51 (31); **HRMS** the compound was not detected.

(1*R,2*S**)-2-Phenyl-1-(1-tosyl-1*H*-indol-3-yl)but-3-en-1-ol (3c).**

Compound **3c** was prepared according to **GP1** from cinnamyl alcohol (0.21 mL, 1.61 mmol) and aldehyde **2c** (321 mg, 1.07 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:4 to 1:3) to afford homoallylic alcohol **3c** (434 mg, 97%) as a viscous colorless oil. $\mathbf{R_f}$ = 0.30 (EtOAc/PE = 1:3); **IR** (film) 3548, 1446, 1365, 1172, 1121, 1019, 972, 907 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3, 1H), 7.59 (br d, *J* = 7.7 Hz, 1H), 7.49 (br d, *J* = 8.4 Hz, 2H), 7.26 – 7.21 (m, 2H), 7.17 (m, 1H), 7.15 – 7.08 (m, 5H), 7.04 – 7.00 (m, 2H), 6.20 (ddd, *J* = 17.1, 10.2, 8.7 Hz, 1H), 5.21 (dd, *J* = 10.1, 1.5 Hz, 1H), 5.14 (ddd, *J* = 17.1, 1.6, 0.8 Hz, 1H), 5.06 (d, *J* = 7.7 Hz, 1H), 3.76 (t^{app}, *J* = 8.2 Hz, 1H), 2.52 (br s, 1H, OH), 2.28 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.6, 140.7, 137.5, 135.0, 134.9, 129.6, 128.9 (2C), 128.4 (2C), 127.9 (2C), 126.5, 124.5, 124.0, 123.1, 123.0, 120.5, 118.4, 113.5, 71.0, 56.7, 21.4; **EI–MS** *m/z* (relative intensity) 299 (13), 155 (30), 116 (11), 91 (100), 89 (15), 65 (25), 63 (10); **HRMS** calcd for $C_{25}H_{23}NO_3SNa$ ($M+Na^+$): 440.12909. Found: 440.12910.

(1*R,2*S**)-1-(2-Chloroquinolin-3-yl)-2-phenylbut-3-en-1-o (3d).**

Compound **3d** was prepared according to **GP1** from cinnamyl alcohol (0.15 mL, 1.17 mmol) and 2-chloroquinoline-3-carbaldehyde (150 mg,

0.783 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:6 to 1:5) to afford homoallylic alcohol **3d** (212 mg, 87%) as a white solid. **mp** 147–152 °C; $\mathbf{R_f}$ = 0.39 (EtOAc/PE = 1:3); **IR** (film) 3341, 1590, 1492, 1396, 1326, 1138, 1039, 921, 752, 727, 699 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.85 (dd, J = 8.1, 1.4 Hz, 1H), 7.72 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.56 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.42 – 7.39 (m, 2H), 7.37 – 7.33 (m, 2H), 7.26 (m, 1H), 6.30 (ddd, J = 17.1, 10.3, 9.1 Hz, 1H), 5.47 (t^{app}, J = 3.8 Hz, 1H), 5.14 (dd, J = 10.3, 1.7 Hz, 1H), 4.91 (ddd, J = 17.2, 1.6, 0.9 Hz, 1H), 3.94 (dd, J = 9.2, 3.8 Hz, 1H), 1.79 (br s, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.6, 146.9 (2C), 141.2, 137.2, 134.4, 133.8, 130.3, 128.8 (2C), 128.2, 128.1 (2C), 127.8, 127.1 (2C), 119.6, 73.8, 54.9; **EI–MS** *m/z* (relative intensity) 169.1 (21), 168.2 (35), 151.2 (45), 142.2 (33), 140.2 (100), 134.3 (34), 132.2 (58), 117.2 (30), 116.1 (62), 115.1 (26), 104.2 (46), 102.2 (37.4), 90.2 (19), 89.2 (40), 78.1 (24), 77.2 (37), 76.1 (29), 75.2 (24), 63.1 (31), 51.1 (56), 50.2 (39); **HRMS** calcd for $C_{19}H_{17}ClNO$ ($M+H^+$): 310.09932. Found: 310.09915.

(1*R,2*S**)-1-(3-Chloro-1-methyl-1*H*-pyrazol-4-yl)-2-phenylbut-3-en-1-ol (3e).**

Compound **3e** was prepared according to **GP1** from cinnamyl alcohol (0.40 mL, 3.11 mmol) and aldehyde **2e** (300 mg, 2.08 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:1) to afford homoallylic alcohol **3e** (529 mg, 97%) as a white solid. **mp** 81–83 °C; $\mathbf{R_f}$ = 0.28 (EtOAc/PE = 1:1); **IR** (film) 3361, 1557, 1407, 1172, 1003, 910 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 7.20 – 7.16 (m, 4H), 6.21 (ddd, J = 17.1, 10.2, 8.8 Hz, 1H), 5.24 (ddd, J = 10.3, 1.6, 0.7 Hz, 1H), 5.19 (ddd, J = 17.1, 1.7, 1.0 Hz, 1H), 4.89 (d, J = 7.0 Hz, 1H), 3.72 (s, 3H), 3.66 (dd, J = 9.1, 6.9 Hz, 1H), 2.46 – 2.36 (br s, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.6, 137.2, 136.8, 130.2, 128.5 (2C), 128.1 (2C), 126.7, 119.6, 118.4, 68.7, 56.8, 39.4; **EI–MS** *m/z* (relative intensity) 246 (22), 245 (15), 244 (68), 210 (14), 209 (100), 208 (16), 194 (17), 168 (14), 145 (79), 144 (21), 143 (21), 142 (46), 141 (20), 140 (14), 139 (17), 131 (32), 129 (80), 52 (17), 51 (47), 50 (14); **HRMS** calcd for $C_{14}H_{16}ClN_2O$ ($M+H^+$): 263.09457. Found: 263.09475.

(1*R,2*S**)-1-(2-Chloropyridin-3-yl)-2-phenylbut-3-en-1-ol (3f).**

Compound **3f** was prepared according to **GP1** from cinnamyl alcohol (0.15 mL, 1.18 mmol) and 2-chloropyridine-3-carbaldehyde (111 mg, 0.784 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:4 to 1:3) to afford homoallylic alcohol **3f** (185 mg, 92%) as a colorless oil. $\mathbf{R_f}$ = 0.33 (EtOAc/PE = 1:3); **IR** (film) 3296, 1579, 1567, 1494, 1452, 1408, 1183, 1120, 1054, 1000, 919 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (dd, J = 4.7, 2.0 Hz, 1H), 7.86 (dd, J = 7.6, 2.0 Hz, 1H), 7.34 – 7.28 (m, 4H), 7.26 – 7.20 (m, 2H), 6.25 (ddd, J = 17.1, 10.2, 9.1 Hz, 1H), 5.29 (t^{app}, J = 3.9 Hz, 1H), 5.15 (dd, J = 10.2, 1.7 Hz, 1H), 4.93 (ddd, J = 17.1, 1.7, 0.9 Hz, 1H), 3.76 (dd, J = 9.2, 4.3 Hz, 1H), 2.69 (d, J = 3.7 Hz, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.7, 148.3, 140.8, 137.6, 136.4, 134.8, 128.7 (2C), 128.0 (2C), 127.0, 122.4, 119.4, 73.5, 55.1; **EI–MS** *m/z* (relative intensity) 118 (100), 117 (93), 115 (55); **HRMS** calcd for $C_{15}H_{15}ClNO$ ($M+H^+$): 260.08367. Found: 260.08397.

(1*R,2*S**)-1-(2-Chloropyridin-3-yl)-2-(2-methoxyphenyl)but-3-en-1-ol (3g).**

Compound **3g** was prepared according to **GP1** from alcohol **1b** (174 mg, 1.06 mmol) and 2-chloropyridine-3-carbaldehyde (100 mg, 0.706 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:4 to 1:3) to afford homoallylic alcohol **3g** (125 mg, 61%) as a yellow oil. $\mathbf{R_f}$ = 0.61 (EtOAc/PE = 1:1); **IR** (film) 3311, 1581, 1567, 1491, 1462, 1409, 1243, 1184, 1052, 1029, 909, 751, 726 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (br d, J = 2.7 Hz, 1H), 7.88 (dd, J = 7.7, 1.9 Hz, 1H), 7.24 (dd, J = 7.6, 1.8 Hz, 1H), 7.21 – 7.17 (m, 2H), 6.90 (td, J = 7.5, 1.1 Hz, 1H), 6.82 (dd, J = 8.2, 1.2 Hz, 1H), 6.29 (ddd, J = 17.1, 10.2, 9.0 Hz, 1H), 5.35 (dd, J = 4.9, 2.0 Hz, 1H), 5.11 (dd, J = 10.2, 1.8 Hz, 1H), 4.96 (ddd, J = 17.1, 1.8, 1.0 Hz, 1H), 4.13 (dd, J = 9.0, 4.9 Hz, 1H), 3.78 (s, 3H), 3.24 (br d, J = 2.9 Hz, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.4, 149.0, 147.9, 137.7, 136.8, 135.1, 129.6, 128.8, 128.1, 122.0, 120.8, 118.6, 110.7, 71.9, 55.2, 50.4; **EI–MS** *m/z* (relative intensity) 289 (0.19), 148 (46), 147 (100), 131 (13), 117 (12), 115 (20), 91 (43), 78 (18), 77 (10), 51 (13); **HRMS** calcd for $C_{16}H_{17}ClNO_2$ ($M+H^+$): 290.09423. Found: 290.09455.

(1*R,2*S**)-1-(2-Chloropyridin-3-yl)-2-(4-methoxyphenyl)but-3-en-1-ol (3h).**

Compound **3h** was prepared according to **GP1** from alcohol **1c** (174 mg, 0.706 mmol) and 2-chloropyridine-3-carbaldehyde (100 mg, 1.06 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:4 to 1:3) to afford homoallylic alcohol **3h** (178 mg, 87%) as a yellow oil. $\mathbf{R_f}$ = 0.58 (EtOAc/PE = 1:1); **IR** (film) 3343, 1609, 1580, 1567, 1510, 1464, 1408, 1245, 1178, 1054, 1034, 910 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (dd, J = 4.8, 2.0 Hz, 1H), 7.86 (ddd, J = 7.7, 2.0 0.6 Hz, 1H), 7.26 – 7.21 (m, 3H), 6.87 – 6.83 (m, 2H); 6.21 (ddd, J = 17.1 10.2, 9.1 Hz, 1H), 5.27 (dd, J = 4.2, 3.0 Hz, 1H), 5.15 (ddd, J = 10.3, 1.7, 0.6 Hz, 1H), 4.94 (ddd, J = 17.1, 1.7, 0.9 Hz, 1H), 3.78 (s, 3H), 3.73 (dd, J = 9.1, 4.6 Hz, 1H), 2.41 (br d, J = 3.5 Hz, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.5, 148.9, 148.2, 137.6, 136.5, 135.2, 132.7, 129.0 (2C), 122.3, 119.0, 114.0 (2C), 73.5, 55.2, 54.3; **EI–MS** *m/z* (relative intensity) 289 (0.5), 148 (14), 147 (10), 115 (15), 91 (26), 78 (14); **HRMS** calcd for $C_{16}H_{17}ClNO_2$ ($M+H^+$): 290.09423. Found: 290.09466.

(1*R,2*S**)-1-(2-Chloropyridin-3-yl)-2-(4-(trifluoromethyl)phenyl)but-3-en-1-ol (3i).**

Compound **3i** was prepared according to **GP1** from alcohol **1d** (257 mg, 1.27 mmol) and 2-chloropyrine-3-carbaldehyde (120 mg, 0.848 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:4 to 1:2) to afford homoallylic alcohol **3i** (146 mg, 53%) as a white solid. **mp** 131–133 °C ; $\mathbf{R_f}$ = 0.29 (EtOAc/PE = 1:3); **IR** (film) 3282, 1617, 1570, 1411, 1324, 1163, 1121, 1068, 1018, 925 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (dd, J = 4.7, 1.9 Hz, 1H), 7.89 (ddd, J = 7.7, 2.0, 0.7 Hz, 1H), 7.61 – 7.57 (m, 2H), 7.50 – 7.46 (m, 2H), 7.28 (m, 1H), 6.25 (ddd, J = 17.2, 10.3, 9.1 Hz, 1H), 5.33 (t^{app}, J = 4.0 Hz, 1H), 5.21 (ddd, J = 10.2, 1.5, 0.6 Hz, 1H), 4.95 (ddd, J = 17.2, 1.5, 0.9 Hz, 1H) 3.82 (dd, J = 9.1, 4.0 Hz, 1H), 2.31 (d, J = 4.0 Hz, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.7, 148.6, 145.2 (d, J = 1.6 Hz), 137.6, 136.2, 133.9, 129.2 (d, J = 32.6 Hz), 128.5 (2C), 125.5 (q, J = 3.8 Hz, 2C), 122.5, 121.2 (d, J = 269 Hz), 120.0, 73.2, 54.8; **EI–MS** *m/z* (relative intensity) 196 (32), 166 (11), 144 (32), 142 (100), 117 (13), 116 (10), 115 (18), 106 (50), 78 (41), 51 (21); **HRMS** calcd for $C_{16}H_{14}ClF_3NO$ ($M+H^+$): 328.07105. Found: 328.07124.

(1*R,2*S**)-2-(4-Methoxyphenyl)-1-phenylbut-3-en-1-ol (3j).**

Compound **3j** was prepared according to **GP1** from alcohol **1c** (1.13 g, 6.89 mmol) and benzaldehyde (0.46 mL, 4.59 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:5) to afford homoallylic alcohol **3j** (1.09 g, 93%) as a yellow oil. $\mathbf{R_f}$ = 0.36 (EtOAc/PE = 1:5); **IR** (film) 3443, 1610, 1583, 1510, 1454, 1302, 1243, 1178, 1033, 917 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 – 7.12 (m 5H), 6.96 (d, J = 8.8 Hz, 2H), 6.74 (d, J = 8.7 Hz, 2H), 6.21 (ddd, J = 17.0 10.2, 8.8 Hz, 1H), 5.27 – 5.17 (m, 2H), 4.80 (d, J = 7.6 Hz, 1H), 3.74 (s, 3H), 3.51 (t, J = 8.3 Hz, 1H), 2.30 (br d, J = 2.5 Hz, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.1, 141.9, 138.0, 132.6, 129.2 (2C), 127.8 (2C), 127.3, 126.7 (2C), 118.0, 113.7 (2C), 77.3, 58.2, 55.1; **EI–MS** *m/z* (relative intensity) 149 (12), 148 (100), 147 (70), 117 (14), 115 (18), 107 (30), 105 (11), 91 (30), 79 (31), 78 (11), 77 (30), 51 (10); **HRMS** calcd for $C_{17}H_{18}O_2Na$ ($M+Na^+$): 277.11990. Found: 277.77996.

(1*R,2*S**)-1-(4-Fluorophenyl)-2-(1-tosyl-1*H*-indol-3-yl)but-3-en-1-ol (3k).**

Compound **3k** was prepared according to **GP1** from alcohol **1e** (266 mg, 0.811 mmol) and *p*-fluorobenzaldehyde (58 µL, 0.541 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:3) to afford a mixture of homoallylic alcohol **3k** and pinacol (78

mg, 32%, 3% pinacol) as a soft white foam. The separation of pinacol was carried out in the subsequent step. R_f = 0.33 (EtOAc/PE = 1:3); **IR** (film) 3547, 1601, 1509, 1446, 1364, 1278, 1219, 1171, 1121, 1093, 1019, 979 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (dt^{app}, J = 8.4, 0.9 Hz, 1H), 7.58 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 7.9 Hz, 1H), 7.29 (s, 1H), 7.26 (m, 1H), 7.18 – 7.13 (m, 3H), 7.09 – 7.04 (m, 2H), 6.79 – 6.73 (m, 2H), 6.16 (ddd, J = 17.1, 10.2, 8.3 Hz, 1H), 5.24 (ddd, J = 10.2, 1.5, 0.8 Hz, 1H), 5.16 (dt^{app}, J = 17.1, 1.3 Hz, 1H), 4.96 (d, J = 7.4 Hz, 1H), 3.75 (t^{app}, J = 8.3 Hz, 1H), 2.49 (br s, 1H, OH), 2.32 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.0 (d, J = 245.5 Hz), 144.8, 137.6, 137.6, 135.8, 134.9, 129.8, 129.7 (2C), 128.0 (d, J = 8.1 Hz, 2C), 126.5 (2C), 124.7, 123.9, 123.0, 121.6, 119.8, 119.0, 114.8 (d, J = 21.3 Hz, 2C), 113.7, 75.0, 49.8, 21.4; **EI–MS** *m/z* (relative intensity) 311 (26), 157 (14), 156 (100), 155 (33), 154 (32), 129 (22), 128 (46), 127 (15), 102 (10), 91 (59), 77 (18), 65 (34), 63 (11), 51 (14); **HRMS** calcd for $C_{25}H_{22}FNO_3SNa$ ($M+Na^+$): 458.11966. Found: 458.11951.

1-((1*R,2*S**)-1-(Allyloxy)-2-phenylbut-3-en-1-yl)-4-fluorobenzene (4a).**

A solution of alcohol **3a** (200 mg, 0.83 mmol, 1 equiv) in THF (2 mL) was added to a suspension of NaH (60% in oil, 51 mg, 1.28 mmol, 1.55 equiv) in THF (1 mL) cooled at 0 °C. The solution was stirred at rt for 1 h. Allyl bromide (0.11 mL, 1.24 mmol, 1.5 equiv) was then added and the solution was stirred at rt for 15 h. Water (1 mL) was added and the product was extracted with Et_2O (3 × 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:99 to 2:98) to afford ether **4a** (181 mg, 77%) as a yellow oil. R_f = 0.36 (EtOAc/PE = 2:98); **IR** (film) 1639, 1603, 1508, 1453, 1418, 1221, 1155, 1077, 990, 918 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 – 7.09 (m, 3H), 7.07 – 7.03 (m, 4H), 6.88 (t^{app}, J = 8.7 Hz, 2H), 6.28 (ddd, J = 17.6, 10.3 and 7.9 Hz, 1H), 5.85 (m, 1H), 5.21 (br d, J = 17.2 Hz, 1H), 5.13 (d, J = 10.3 Hz, 2H), 4.99 (d, J = 17.2 Hz, 1H), 4.51 (d, J = 7.2 Hz, 1H), 3.92 (dd, J = 13.0, 4.5 Hz, 1H), 3.72 (dd, J = 13.0, 6.0 Hz, 1H), 3.53 (t^{app}, J = 7.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.0 (d, J = 245.2 Hz), 141.2, 138.1, 136.1 (d, J = 3.1 Hz), 134.6, 128.9 (d, J = 8.0 Hz, 2C), 128.6 (2C), 128.1 (2C), 126.4, 116.6 (2C), 114.8 (d, J = 21.2 Hz, 2C), 83.9, 69.6, 57.5; **EI–MS** *m/z* (relative intensity) 165 (75), 123 (100), 117 (20), 115 (30), 109 (34), 91 (20) ; **HRMS** the compound was not detected.

3-((1*R,2*S**)-1-(Allyloxy)-2-phenylbut-3-en-1-yl)-1-tosyl-1*H*-indole (4c).**

NaH (60% in oil, 14 mg, 0.36 mmol, 1.55 equiv) was added to a solution of alcohol **3c** (96 mg, 0.23 mmol, 1 equiv) in THF (0.9 mL) cooled at 0 °C. The solution was stirred at rt for 1 h. Allyl bromide (30 µL, 0.34 mmol, 1.5 equiv) was added and the solution was stirred at rt for 90 h. Water (1 mL) was added and the product was extracted with Et_2O (3 × 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:9 to 1:8) to afford ether **4c** (48 mg, 45%) as a slightly pink oil. R_f = 0.40 (EtOAc/PE = 1:7); **IR** (film) 1598, 1446, 1367, 1268, 1173, 1121, 1085, 976, 909 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (dt^{app}, J = 8.2, 0.8 Hz, 1H), 7.64 (ddd, J = 7.9, 1.2, 0.7 Hz, 1H), 7.48 (br d^{app}, J = 8.4 Hz, 2H), 7.26 (ddd, J = 8.3, 7.2, 1.6 Hz, 1H), 7.21 – 7.14 (m, 4H), 7.13 – 7.09 (m, 3H), 7.02 – 6.98 (m, 2H), 6.29 (ddd, J = 17.2, 10.3, 7.8 Hz, 1H), 5.84 (dddd, J = 16.4, 10.8, 6.1, 4.9 Hz, 1H), 5.19 (dq^{app}, J = 17.2, 1.7 Hz, 1H), 5.16 – 5.11 (m, 2H), 4.96 (dt^{app}, J = 17.2, 1.2 Hz, 1H), 4.79 (d, J = 7.8 Hz, 1H), 3.95 (ddt^{app}, J = 13.0, 4.9, 1.6 Hz, 1H), 3.82 – 3.73 (m, 2H), 2.35 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.6, 141.3, 138.2, 135.2, 135.0, 134.6, 129.7 (2C), 129.2, 128.3 (2C), 128.2 (2C), 126.6 (2C), 126.4, 124.9, 124.5, 123.0, 121.3, 120.7, 116.8, 116.7, 113.5, 78.3, 69.7, 55.3, 21.5; **HRMS** calcd for $C_{28}H_{27}NO_3SNa$ ($M+Na^+$): 480.16039. Found: 480.16016.g

3-((1*R,2*S**)-1-(Allyloxy)-2-phenylbut-3-en-1-yl)-2-chloropyridine (4f).**

NaH (60% in oil, 11 mg, 0.29 mmol, 1.55 equiv) was added to a solution of alcohol **3f** (48 mg, 0.18 mmol, 1 equiv) in THF (0.7 mL) and the solution was stirred at rt for 1 h. Allyl bromide (24 µL, 0.28 mmol, 1.5 equiv) was added and the solution was stirred at rt for 15 h. The reaction mixture was quenched with H_2O (1 mL) then it was extracted with Et_2O (3 × 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 17:83 to 25:75) to afford ether **4f** (33 mg, 59%) as a yellow oil. **Rf** 0.66 (EtOAc/PE = 1:5); **IR** (film) 1639, 1601, 1579, 1563, 1494, 1453, 1407, 1335, 1182, 1119, 1088, 1059, 998, 920 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (dd, J = 4.7, 2.0 Hz, 1H), 7.78 (dd, J = 7.5, 1.9 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.32 – 7.20 (m, 4H), 6.27 (ddd, J = 17.2, 10.2, 8.9 Hz, 1H), 5.74 (ddt, J = 17.2, 10.6 and 5.4 Hz, 1H), 5.18 (dq^{app}, J = 17.2, 1.7 Hz, 1H), 5.13 – 5.06 (m, 2H), 4.99 (d, J = 3.7 Hz, 1H), 4.78 (ddd, J = 17.2, 1.8, 1.0 Hz, 1H), 3.85 (ddt, J = 12.9, 5.2, 1.5 Hz, 1H), 3.71 (ddt, J = 12.9, 5.7, 1.5 Hz, 1H), 3.62 (dd, J = 8.9, 3.7 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.8, 148.4 141.6, 137.8, 135.5, 135.1, 134.0, 128.3 (2C), 128.2 (2C), 126.7, 122.3, 118.0, 117.0, 80.6, 70.6, 54.8; **EI–MS** *m/z* (relative intensity) 184 (32), 182 (100), 140 (32), 117 (55), 116 (17), 115 (60), 91 (30); **HRMS** calcd for $C_{18}H_{19}ClNO$ ($M+H^+$): 300.11497. Found: 300.11503.

3-((1*R,2*S**)-1-(Allyloxy)-2-(2-methoxyphenyl)but-3-en-1-yl)-2-chloropyridine (4g).**

NaH (60% in oil, 12 mg, 0.296 mmol, 1.55 equiv) was added to a solution of alcohol **3g** (55 mg, 0.191 mmol, 1 equiv) in THF (0.72 mL) cooled at 0 °C. The solution was stirred at rt for 1 h, then allyl bromide (25 µL, 0.286 mmol, 1.5 equiv) was added to the solution. After stirring for 38 h, H_2O (1 mL) was added to the reaction mixture and the product was extracted with Et_2O (3 × 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:5) to afford ether **4g** (43 mg, 69%) as a colorless oil R_f = 0.61 (EtOAc/PE = 1:3); **IR** (film) 1599, 1580, 1563, 1491, 1462, 1408 1333, 1289, 1243, 1183, 1082, 1058, 1030, 999, 921 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.23 (dd, J = 4.7, 2.0 Hz, 1H), 7.84 (dd, J = 7.6, 2.0 Hz, 1H), 7.34 (dd, J = 7.6, 1.7 Hz, 1H), 7.21 (dd, J = 7.7, 4.6 Hz, 1H), 7.15 (ddd, J = 8.2, 7.4, 1.7 Hz, 1H), 6.87 (td^{app}, J = 7.5, 1.2 Hz, 1H), 6.76 (dd, J = 8.2, 1.1 Hz, 1H), 6.31 (ddd, J = 17.1, 10.2, 8.6 Hz, 1H), 5.74 (dddd, J = 17.2, 10.5, 5.8, 5.2 Hz, 1H), 5.18 (dq^{app}, J = 17.2, 1.7 Hz, 1H), 5.12 – 5.04 (m, 3H), 4.89 (ddd, J = 17.2, 1.8, 1.1 Hz, 1H), 4.19 (dd, J = 8.6, 5.5 Hz, 1H), 3.84 (ddt, J = 12.9, 5.2, 1.5 Hz, 1H), 3.74 (s, 3H) ; 3.74 – 3.60 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.3, 150.1, 148.3, 138.1, 136.5, 135.5, 134.2, 129.5, 129.1, 127.6, 122.0, 120.3, 117.4, 116.9, 110.3, 79.1, 70.4, 55.1, 47.5; **EI–MS** *m/z* (relative intensity) 329 (0.37), 184 (20), 182 (63), 148 (11), 147 (100), 140 (17), 134 (11), 131 (15), 115 (20), 91 (40), 78 (10), 77 (10); **HRMS** calcd for $C_{19}H_{21}ClNO_2$ ($M+H^+$): 330.12553. Found: 330.12562.

3-((1*R,2*S**)-1-(Allyloxy)-2-(4-methoxyphenyl)but-3-en-1-yl)-2-chloropyridine (4h).**

NaH (60% in oil, 12 mg, 0.310 mmol, 1.55 equiv) was added to a solution of alcohol **3h** (58 mg, 0.200 mmol, 1 equiv) in THF (0.76 mL) cooled at 0 °C. The solution was stirred at rt for 1 h and allyl bromide (26 µL, 0.300 mmol, 1.5 equiv) was added. The solution was stirred at rt for 63 h, quenched with H_2O (1 mL) and the product was extracted with Et_2O (3 × 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:6) to afford ether **4h** (55 mg, 83%) as a colorless oil. R_f = 0.40 (EtOAc/PE = 1:5); **IR** (film) 1610, 1579, 1563, 1510, 1463, 1408, 1337, 1247, 1179, 1059, 1035, 998, 920 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (dd, J = 4.7, 2.0 Hz, 1H), 7.77 (ddd, J = 7.6, 2.0, 0.6 Hz, 1H), 7.28 – 7.23 (m, 3H), 6.83 (d^{app}, J = 8.9 Hz, 2H), 6.23 (ddd, J = 17.1, 10.2, 8.8 Hz, 1H), 5.76 (dddd, J = 17.2, 10.4, 5.7, 5.2 Hz, 1H), 5.20 (app dq, J = 17.2, 1.5 Hz, 1H), 5.12 (dq^{app}, J = 10.4, 1.5 Hz, 1H), 5.06 (ddd, J = 10.2, 1.8, 0.7 Hz, 1H), 4.95 (br d, J = 3.9 Hz, 1H), 4.77 (ddd, J = 17.2, 1.7, 1.0 Hz, 1H), 3.85 (ddt^{app}, J = 12.9, 5.2, 1.5 Hz, 1H), 3.79 (s, 3H), 3.72 (ddt^{app}, J = 12.8, 5.7, 1.5 Hz, 1H), 3.57 (dd, J = 8.8, 3.9 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.4, 149.9, 148.4, 137.8, 135.9, 135.2, 134.0, 133.7, 129.2 (2C), 122.3, 117.7, 117.0, 113.7 (2C), 80.7, 70.6, 55.2, 54.0; **EI–MS** *m/z* (relative intensity) 329

(0.16), 182 (10), 148 (11), 147 (100), 115 (10), 91 (18); **HRMS** calcd for $C_{19}H_{21}ClNO_2$ (M+H$^+$): 330.12553. Found: 330.12578.

3-((1*R,2*S**)-1-(Allyloxy)-2-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)-2-chloropyridine (4i).**

NaH (60% in oil, 11 mg, 0.286 mmol, 1.55 equiv) was added to a solution of alcohol **3i** (60 mg, 0.184 mmol, 1 equiv) in THF (0.70 mL) cooled at 0 °C. The solution was stirred at rt for 1 h and allyl bromide (24 µL, 0.276 mmol, 1.5 equiv) was added. After 60 h at rt, H_2O (1 mL) was added and the product was extracted with Et_2O (3 × 3 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:5) to afford ether **4i** (21 mg, 32%) as a colorless oil. **R_f** = 0.27 (EtOAc/PE = 1:5); **IR** (film) 1618, 1565, 1409, 1325, 1123, 1068, 1018, 925 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 4.7, 2.0 Hz, 1H), 7.78 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.58 (br d, *J* = 8.1 Hz, 2H), 7.50 (br d, *J* = 8.1 Hz, 2H), 7.28 (m, 1H), 6.25 (ddd, *J* = 17.2, 10.2, 9.0 Hz, 1H), 5.73 (dddd, *J* = 17.2, 10.6, 5.8, 5.2 Hz, 1H), 5.19 (dq^{app}, *J* = 17.2, 1.7 Hz, 1H), 5.15 – 5.08 (m, 2H), 4.96 (d, *J* = 3.2 Hz, 1H), 4.78 (dt^{app}, *J* = 17.1, 1.3 Hz, 1H), 3.87 (ddt, *J* = 12.8, 5.2, 1.5 Hz, 1H), 3.72 – 3.65 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6, 148.7, 145.8, 137.7, 134.6, 134.4, 133.7, 129.0 (d, *J* = 32.2 Hz), 128.6 (2C), 125.2 (q, *J* = 3.8 Hz, 2C), 124.2 (d, *J* = 272 Hz), 122.4, 119.0, 117.4, 80.2, 70.6, 54.5; **EI–MS** *m/z* (relative intensity) 185 (16), 184 (32), 183 (11), 182 (100), 165 (15), 142 (10), 140 (25), 116 (12), 115 (17); **HRMS** calcd for $C_{19}H_{18}ClF_3NO$ (M+H$^+$): 368.10235. Found: 368.10270.

3-((1*R,2*S**)-1-(Allyloxy)-1-(4-fluorophenyl)but-3-en-2-yl)-1-tosyl-1*H*-indole (4k).**

NaH (60% in oil, 10 mg, 0.240 mmol, 1.55 equiv) was added to a solution of alcohol **3k** (67 mg, 0.155 mmol, 1 equiv) in THF (0.59 mL) cooled at 0 °C. The solution was stirred at rt for 1 h and allyl bromide (20 µL, 0.232 mmol, 1.5 equiv) was added. After stirring the solution at rt for 18 h, H_2O (1 mL) was added to the reaction mixture and the product was extracted with Et_2O (3 × 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:9 to 1:3) to afford ether **4k** (19 mg, 26%) as a colorless oil and the recovered starting material **3k** (32 mg, 47%) was isolated as an orange oil. **R_f** = 0.44 (EtOAc/PE = 1:5); **IR** (film) 1602, 1508, 1446, 1368, 1278, 1173, 1121, 1086, 983, 918 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (br d, *J* = 8.3 Hz, 1H), 7.58 (d^{app}, *J* = 8.3 Hz, 2H), 7.44 (br d, *J* = 8.1 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.24 (s, 1H), 7.20 – 7.15 (m, 3H), 7.06 – 7.01 (m, 2H), 6.82 – 6.76 (m, 2H), 6.24 (ddd, *J* = 17.4, 10.3, 7.3 Hz, 1H), 5.86 (dddd, *J* = 17.3, 10.8, 6.0, 5.0 Hz, 1H), 5.23 (dq^{app}, *J* = 17.2, 1.7 Hz, 1H), 5.16 (dq^{app}, *J* = 10.8, 1.6 Hz, 1H), 5.12 (dt^{app}, *J* = 10.3, 1.3 Hz, 1H), 4.95 (dt^{app}, *J* = 17.2, 1.4 Hz, 1H), 4.63 (d, *J* = 7.0 Hz, 1H), 3.92 (ddt, *J* = 12.9, 5.0, 1.6 Hz, 1H), 3.79 (m, 1H), 3.73 (ddt^{app}, *J* = 12.9, 6.0, 1.4 Hz, 1H), 2.35 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.0 (d, *J* = 245.3 Hz), 144.7, 136.2, 135.9 (d, *J* = 3.2 Hz), 135.2, 135.0, 134.4, 130.1, 129.7 (2C), 128.7 (d, *J* = 8.0 Hz, 2C), 126.6 (2C), 124.5, 124.2, 122.8, 121.9, 120.2, 117.2, 116.9, 114.8 (d, *J* = 21.3 Hz, 2C), 113.6, 82.6, 69.8, 48.3, 21.5; **EI–MS** *m/z* (relative intensity) 310 (13), 262 (21), 261 (10), 260 (12), 166 (10), 165 (71), 155 (27), 154 (41), 128 (10), 127 (10), 124 (17), 123 (74), 109 (20), 95 (18), 91 (100), 75 (10), 65 (26), 57 (28); **HRMS** calcd for $C_{28}H_{26}FNO_3SNa$ (M+Na$^+$): 498.15096. Found: 498.15037.

(2*R,3*S**)-2-(4-Fluorophenyl)-3-phenyl-3,6-dihydro-2*H*-pyran (5a).**

The 2nd generation Grubbs catalyst (6.7 mg, 7.88 µmol, 2 mol %) was added to a solution of diene **4a** (111 mg, 0.39 mmol, 1 equiv) in degassed CH_2Cl_2 (1.9 mL). The solution was stirred at rt for 4 h, then it was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 3:97) to afford dihydropyran **5a** (97 mg, 97%) as a yellow oil. **R_f** = 0.40 (EtOAc/PE = 2:98); **IR** (film) 1505, 1510, 1452, 1222, 1157, 1114, 1049, 1025, 829 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 3H), 7.03 – 6.98 (m, 2H), 6.92 – 6.86 (m, 4H), 6.03 (m, 1H), 5.93 (dq^{app}, *J* = 10.2, 2.0 Hz, 1H), 4.51 – 4.39 (m, 2H), 4.31 (d, *J* = 9.2 Hz, 1H), 3.54 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.1 (d, *J* = 245.3 Hz), 140.5, 136.3 (d, *J* = 3.2 Hz), 128.9, 128.6 (2C), 128.5 (d, *J* = 8.0 Hz, 2C), 128.2 (2C), 126.7, 126.4, 114.7 (d, *J* = 21.2 Hz, 2C), 82.6, 66.4, 49.2; **EI–MS** *m/z* (relative intensity) 130 (100), 129 (62), 128 (20), 115 (30); **HRMS** the product was not detected.

3-((2*R,3*S**)-3-Phenyl-3,6-dihydro-2*H*-pyran-2-yl)-1-tosyl-1*H*-indole (5c).**

The 2nd generation Grubbs catalyst (1.5 mg, 1.75 µmol, 2 mol %) was added to a solution of diene **4c** (40 mg, 0.087 mmol, 1 equiv) in degassed CH_2Cl_2 (0.42 mL). After 23 h at rt, the solution was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:9 to 1:7) to afford dihydropyran **5c** (32 mg, 85%) as a slightly yellow oil. **R_f** = 0.27 (EtOAc/PE = 1:7); **IR** (film) 1597, 1447, 1366, 1273, 1172, 1122, 1094, 1022, 979, 909 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (dt^{app}, *J* = 8.4, 0.9 Hz, 1H), 7.59 (br d, *J* = 8.4 Hz, 2H), 7.51 (br d, *J* = 7.9 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.21 (s, 1H), 7.19 – 7.12 (m, 6H), 6.94 – 6.91 (m, 2H), 6.04 (ddt^{app}, *J* = 10.3, 3.3, 2.0 Hz, 1H), 5.95 (dq^{app}, *J* = 10.3, 2.1 Hz, 1H), 4.64 (d, *J* = 8.6 Hz, 1H), 4.45 (ddt^{app}, *J* = 16.7, 4.0, 2.0 Hz, 1H), 4.35 (dddd, *J* = 16.7, 5.1, 3.0, 2.0 Hz, 1H), 3.85 (m, 1H), 2.35 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.7, 140.9, 135.1, 135.0, 129.7 (2C), 129.3, 128.4, 128.4 (2C), 128.3 (2C), 126.8, 126.7 (2C), 126.4, 124.6, 124.1, 123.1, 121.4, 120.8, 113.4, 76.5, 65.7, 46.7, 21.5; **HRMS** calcd for $C_{26}H_{23}NO_3SNa$ (M+Na$^+$): 452.12909. Found: 452.12916.

2-Chloro-3-((2*R,3*S**)-3-phenyl-3,6-dihydro-2*H*-pyran-2-yl)pyridine (5f).**

The 2nd generation Grubbs catalyst (1.7 mg, 2.06 µmol, 2 mol %) was added to a solution of diene **4f** (31 mg, 0.10 mmol, 1 equiv) in degassed CH_2Cl_2 (0.49 mL). After 8 h at rt, a second portion of Grubbs 2nd generation catalyst (1.7 mg, 2.06 µmol, 2 mol %) was added. After another 15 h, the solution was concentrated under reduced pressure and the crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:5) to afford dihydropyran **5f** (27 mg, 98%) as a yellow oil. **R_f** = 0.32 (EtOAc/PE = 1:5); **IR** (film) 1584, 1565, 1492, 1463, 1415, 1341 1288, 1244, 1190, 1179, 1109, 1071, 1050, 1026, 916 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 4.7, 2.0 Hz, 1H), 7.96 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.29 (dd, *J* = 7.7, 4.7 Hz, 1H), 7.20 – 7.17 (m, 3H), 6.93 – 6.89 (m, 2H), 6.06 (m, 1H), 5.98 (dq^{app}, *J* = 10.2, 2.0 Hz, 1H), 4.86 (d, *J* = 9.3 Hz, 1H), 4.50 (dddd, *J* = 16.8, 4.1, 2.3, 1.7 Hz, 1H), 4.41 (dddd, *J* = 16.7, 3.0, 3.3, 1.9 Hz, 1H), 3.62 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.6, 148.7, 139.0, 137.6, 135.0, 128.7, 128.5 (2C), 128.4 (2C), 127.1, 126.5, 122.7, 78.0, 66.5, 48.6; **EI–MS** *m/z* (relative intensity) 130 (100), 129 (55) 128 (17), 115 (25); **HRMS** calcd for $C_{16}H_{15}ClNO$ (M+H$^+$): 272.08702. Found: 272.08403.

2-Chloro-3-((2*R,3*S**)-3-(2-methoxyphenyl)-3,6-dihydro-2*H*-pyran-2-yl)pyridine (5g).**

The 2nd generation Grubbs catalyst (2.5 mg, 2.95 µmol, 2 mol %) was added to a solution of diene **4g** (43 mg, 0.131 mmol, 1 equiv) in degassed CH_2Cl_2 (0.70 mL). After stirring at rt for 22 h then refluxed for 8 h, the solution was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:4) to afford dihydropyran **5g** (36 mg, 90%) as a colorless oil. **R_f** = 0.38 (EtOAc/PE = 1:3); **IR** (film) 1584, 1565, 1493, 1463, 1416, 1341, 1288, 1245, 1190, 1179, 1109, 1071, 1051, 1027, 916 cm^{-1};**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 4.7, 2.0 Hz, 1H), 7.99 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.25 (ddd, *J* = 7.6, 4.7, 0.5 Hz, 1H), 7.20 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.16 (ddd, *J* = 8.2, 7.4, 1.8 Hz, 1H), 6.90 (td^{app}, *J* = 7.5, 1.1 Hz, 1H), 6.64 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.01 (dddd, *J* = 10.3, 3.4, 2.6, 1.8 Hz, 1H), 5.89 (dq^{app}, *J* = 10.3, 2.1 Hz, 1H), 4.86 (d, *J* = 9.2 Hz, 1H), 4.49 (dddd, *J* = 16.6, 4.1, 2.4, 1.8 Hz, 1H), 4.39 (dddd, *J* = 16.6, 3.4, 3.0, 2.0 Hz, 1H),

4.22 (m, 1H), 3.35 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.7, 150.1, 148.3, 138.2, 135.4, 129.3, 129.2, 128.2, 127.5, 125.9, 122.2, 120.7, 110.2, 77.8, 66.4, 54.7, 40.1; **EI–MS** *m/z* (relative intensity) 302 (0.03), 161 (12), 160 (100), 159 (57), 145 (21), 144 (18), 129 (46), 128 (17), 127 (10), 117 (12), 115 (24), 91 (17); **HRMS** calcd for $C_{17}H_{17}ClNO_2$ ($M+H^+$): 302.09423. Found: 302.09452.

2-Chloro-3-((2*R,3*S**)-3-(4-methoxyphenyl)-3,6-dihydro-2*H*-pyran-2-yl)pyridine (5h).**

The Grubbs 2nd generation catalyst (5.5 mg, 6.50 µmol, 4 mol %) was added to a solution of diene **4h** (54 mg, 0.163 mmol, 1 equiv) in degassed CH_2Cl_2 (0.87 mL). The solution was stirred at rt for 24 h and then concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:5) to afford dihydropyran **5h** (45 mg, 92%) as a slightly brown oil. $\mathbf{R_f}$ = 0.27 (EtOAc/PE = 1:5); **IR** (film) 1612, 1583, 1566, 1510, 1415, 1380, 1302, 1246, 1176, 1109, 1033, 909 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 4.7, 2.0 Hz, 1H), 7.95 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.28 (dd, *J* = 8.1, 4.9 Hz, 1H), 6.86 (d^{app}, *J* = 8.7 Hz, 2H), 6.72 (d^{app}, *J* = 8.7 Hz,2H), 6.03 (dddd, *J* = 10.2, 3.3, 2.5, 1.6 Hz, 1H), 5.95 (dq^{app}, *J* = 10.3, 1.8 Hz, 1H), 4.82 (d, *J* = 9.2 Hz, 1H), 4.48 (dddd, *J* = 16.7, 4.1, 2.3, 1.7 Hz, 1H), 4.39 (dddd, *J* = 16.7, 3.2, 3.0, 1.9 Hz, 1H), 3.73 (s, 3H), 3.57 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.6, 150.6, 148.6, 137.6, 135.1, 131.0, 129.4 (2C), 129.0, 126.3, 122.6, 113.8 (2C), 78.2, 66.5, 55.1, 47.7; **EI–MS** *m/z* (relative intensity) 301 (0.07), 161 (11), 160 (100), 159 (43), 145 (18), 144 (18), 129 (36), 128 (13), 117 (16), 115 (19), 91 (13); **HRMS** calcd for $C_{17}H_{17}ClNO_2$ ($M+H^+$): 302.09423. Found: 302.09474.

2-Chloro-3-((2*R,3*S**)-3-(4-(trifluoromethyl)phenyl)-3,6-dihydro-2*H*-pyran-2-yl)pyridine (5i).**

The 2nd generation Grubbs catalyst (1.9 mg, 2.19 µmol, 4 mol %) was added to a solution of diene **4i** (20 mg, 54.7 µmol, 1 equiv) in degassed CH_2Cl_2 (0.29 mL). The solution was stirred at rt for 26 h, then concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:6) to afford dihydropyran **5i** (16 mg, 87%) as a colorless oil. $\mathbf{R_f}$ = 0.25 (EtOAc/PE = 1:5); **IR** (film) 1619, 1566, 1416, 1324, 1164, 1112, 1068, 1018 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 4.7, 2.0 Hz, 1H), 7.97 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.45 (br d, *J* = 8.0 Hz, 2H), 7.32 (dd, *J* = 7.7, 4.7 Hz, 1H), 7.04 (br d, *J* = 7.9 Hz, 2H), 6.12 (dddd, *J* = 10.2, 3.4, 2.5, 1.8 Hz, 1H), 5.95 (dq^{app}, *J* = 10.3, 2.2 Hz, 1H), 4.86 (d, *J* = 9.2 Hz, 1H), 4.52 (dddd, *J* = 16.8, 4.0, 2.4, 1.8 Hz, 1H), 4.43 (dq^{app}, *J* = 16.9, 2.7 Hz, 1H), 3.68 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.4, 149.0, 143.2, 137.6, 134.6, 129.5 (d, *J* = 32.5 Hz), 128.9 (2C), 127.7, 127.3, 125.4 (q, *J* = 3.9 Hz, 2C), 124.2 (d, *J* = 276 Hz), 122.8, 77.7, 66.5, 48.7; **EI–MS** *m/z* (relative intensity) 198 (44), 130 (11), 129 (100), 128 (17); **HRMS** calcd for $C_{17}H_{14}ClF_3NO$ ($M+H^+$): 340.07105. Found: 340.07112.

3-((2*R,3S*)-2-(4-Fluorophenyl)-3,6-dihydro-2*H*-pyran-3-yl)-1-tosyl-1*H*-indole (5k).**

The 2nd generation Grubbs catalyst (0.58 mg, 0.685 µmol, 2 mol %) was added to a solution of diene **4k** (16 mg, 34.3 µmol, 1 equiv) in degassed CH_2Cl_2 (0.16 mL). The solution was stirred at rt for 25 h, then concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:9 to 1:7) to afford dihydropyran **5k** (14 mg, 93%) as a colorless oil. $\mathbf{R_f}$ 0.23 (EtOAc/PE, 1:7); **IR** (film) 1603, 1511, 1446, 1368, 198, 1224, 1173, 1119, 1094, 1048, 1023, 973 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.3 Hz, 1H), 7.59 (br d, *J* = 8.4 Hz, 2H), 7.25 (m, 1H), 7.21 – 7.15 (m, 3H), 7.13 (s, 1H), 7.08 (m, 1H), 6.93 – 6.87 (m, 2H), 6.75 – 6.70 (m, 2H), 6.03 (dq^{app}, *J* = 10.2, 2.8 Hz, 1H), 5.93 (dq^{app}, *J* = 10.0, 2.0 Hz, 1H), 4.54 – 4.43 (m, 3H), 3.73 (m, 1H), 2.36 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.1 (d, *J* = 245.5 Hz), 144.8, 136.4 (d, *J* = 3.1 Hz), 135.2, 135.2, 129.9, 129.7 (2C), 128.2 (d, *J* = 8.0 Hz, 2C), 128.1, 126.63 (2C), 126.60, 124.6, 124.2, 122.9, 121.9, 119.9, 114.8 (d, *J* = 21.3 Hz, 2C), 113.7, 80.5, 66.5, 40.8, 21.5; **EI–MS** *m/z* (relative intensity) 220 (27), 206 (17), 205 (100), 177 (12), 145 (14), 105 (12), 91 (12), 81 (14), 67 (12), 57 (48), 55 (14); **HRMS** calcd for $C_{26}H_{22}FNO_3SNa$ ($M+Na^+$): 470.11966. Found: 470.11967.

(1*R,2*S**)-1-(4,6-Dichloropyrimidin-5-yl)-2-phenylbut-3-en-1-yl acrylate (6b).**

This compound was prepared according to **GP2** from alcohol **3b** (371 mg, 1.26 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:5) to afford ester **6b** (187 mg, 43%) as a white solid. **mp** 62–63 °C; $\mathbf{R_f}$ = 0.80 (EtOAc/PE = 1:3); **IR** (film) 1727, 1537, 1514, 1415, 1404, 1360, 1338, 1295, 1255, 1215, 1173, 1132, 1045, 984 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.22 – 7.13 (m, 5H), 6.59 (d, *J* = 10.6 Hz, 1H), 6.50 (dd, *J* = 17.3, 1.3 Hz, 1H), 6.25 – 6.14 (m, 2H), 5.92 (dd, *J* = 10.4, 1.3 Hz, 1H), 5.26 (m, 1H), 5.23 (m, 1H), 4.49 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.0, 156.6 (3C), 137.6, 136.6, 132.3, 129.0, 128.6 (2C), 128.0 (2C), 127.7, 127.4, 118.1, 72.8, 51.3; **EI–MS** *m/z* (relative intensity) 117 (78), 115 (25), 91 (10), 55 (100); **HRMS** calcd for $C_{17}H_{15}Cl_2N_2O_2$ ($M+H^+$): 349.05051. Found: 349.05053.

(1*R,2*S**)-1-(2-Chloroquinolin-3-yl)-2-phenylbut-3-en-1-yl acrylate (6d).**

This compound was prepared according to **GP2** using alcohol **3d** (423 mg, 1.36 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:3) to afford ester **6d** (201 mg, 41%) as a colorless oil. $\mathbf{R_f}$ = 0.54 (EtOAc/PE = 1:5); **IR** (film) 1726, 1619, 1592, 1562, 1490, 1453, 1402, 1330, 1294, 1258, 1169, 1137, 1039, 981 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.68 (ddd, *J* = 8.6, 7.0, 1.6 Hz, 1H), 7.51 (t^{app}, *J* = 7.0 Hz, 1H), 7.32 – 7.24 (m, 4H), 7.19 (m, 1H), 6.60 (d, *J* = 5.0 Hz, 1H), 6.47 (dd, *J* = 17.3, 1.3 Hz, 1H), 6.29 (ddd, *J* = 17.1, 10.2, 9.0 Hz, 1H), 6.21 (dd *J* = 17.3, 10.4 Hz, 1H), 5.89 (dd, *J* = 10.4, 1.3 Hz, 1H), 5.15 (dd, *J* = 10.2, 1.6 Hz, 1H), 4.95 (dt^{app}, *J* = 17.0, 1.2 Hz, 1H), 4.04 (dd, *J* = 9.0, 5.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.5, 148.5, 146.9, 139.7, 136.9, 134.7, 131.8, 131.0, 130.5, 128.5 (2C), 128.1, 128.0 (2C), 127.7, 127.5, 127.1, 127.0, 126.6, 119.1, 75.0, 53.8; **EI–MS** *m/z* (relative intensity) 291 (10), 192 (21), 117 (32), 115 (15), 55 (100); **HRMS** calcd for $C_{22}H_{18}ClNO_2Na$ ($M+Na^+$): 386.09183. Found: 386.09205.

(1*R,2*S**)-1-(3-chloro-1-methyl-1*H*-pyrazol-4-yl)-2-phenylbut-3-en-1-yl acrylate (6e).**

This compound was prepared according to **GP2** from alcohol **3e** (369 mg 0.998 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:5 to 1:1) to afford ester **6e** (278 mg, 88%) as a colorless oil. $\mathbf{R_f}$ = 0.62 (EtOAc/PE = 1:1); **IR** (film) 1722, 1638, 1560, 1405, 1295, 1269, 1179, 1043, 984, 969 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 2H), 7.20 – 7.15 (m, 3H), 7.04 (s, 1H), 6.42 (dd, *J* = 17.3, 1.5 Hz, 1H), 6.15 – 6.05 (m, 3H), 5.84 (dd, *J* = 10.4, 1.4 Hz, 1H) 5.15 (br s, 1H), 5.12 (ddd, *J* = 8.2, 1.5, 0.8 Hz, 1H), 3.97 (t^{app}, *J* = 8.6 Hz, 1H), 3.70 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.9, 139.6, 137.3, 137.1, 131.1, 131.0, 128.4 (2C), 128.2, 128.1 (2C), 126.8, 117.5, 116.1, 69.7, 54.2, 39.3; **EI–MS** *m/z* (relative intensity) 244 (15), 209 (22), 199 (11), 129 (21), 115 (13), 72 (13), 55 (100); **HRMS** calcd for $C_{17}H_{18}ClN_2O_2$ ($M+H^+$): 317.10513. Found: 317.10513.

(5*S,6*R**)-6-(4,6-dichloropyrimidin-5-yl)-5-phenyl-5,6-dihydro-2*H*-pyran-2-one (7b).**

A solution of diene **6b** (106 mg, 0.304 mmol, 1 equiv) and 2nd generation Hoveyda-Grubbs catalyst (7.6 mg, 12.1 µmol, 4 mol %) in CH_2Cl_2 (1.5 mL) was heated at 60 °C in a sealed tube. After 48 h, the solution was concentrated under reduced pressure and the crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:5) to afford lactone **7b** (62 mg, 64%) as a white solid. **mp** 163–165 °C; $\mathbf{R_f}$ = 0.19 (EtOAc/PE = 1:5 ; **IR** (film) 1735, 1541, 1515, 1416, 1369, 1242, 1210, 1162, 1054, 1041, 925 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.69 (s, 1H),

7.34 – 7.26 (m, 3H), 7.06 (dd, *J* = 9.9, 2.0 Hz, 1H), 7.03 – 7.00 (m, 2H), 6.33 (dd, *J* = 9.9, 2.9 Hz, 1H), 6.09 (d, *J* = 12.2 Hz, 1H), 4.71 (ddd, *J* = 12.2, 2.8, 1.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 162.2, 162.0 (2C), 157.5, 149.1, 135.5, 129.2 (2C), 128.7, 128.4 (2C), 126.7, 121.2, 79.4, 42.7; **EI–MS** *m/z* (relative intensity) 145 (12), 144 (100), 116 (51), 115 (59); **HRMS** calcd for $C_{15}H_{10}Cl_2N_2O_2Na$ ($M+Na^+$): 343.00115. Found: 343.00112.

(5*S,6*R**)-6-(2-Chloroquinolin-3-yl)-5-phenyl-5,6-dihydro-2*H*-pyran-2-one (7d).**

A solution of diene **6d** (235 mg, 0.645 mmol, 1 equiv) and 2nd generation Hoveyda-Grubbs catalyst (12 mg, 19.4 µmol, 4 mol %) in toluene (5 mL) was heated at 100 °C. After 21 h, the solution was concentrated under reduced pressure and the crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:3 to 1:2) to afford lactone **7d** (137 mg, 63%) as a white solid. **mp** 146–149 °C; **R_f** = 0.16 (EtOAc/PE = 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.35 (s, 1H), 7.99 (d, *J* = 8.5 Hz, 1H), 7.87 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.77 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.61 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.30 – 7.25 (m, 3H), 7.09 – 7.05 (m, 2H), 7.00 (dd, *J* = 9.8, 3.0 Hz, 1H), 6.36 (dd, *J* = 9.8, 2.4 Hz, 1H), 6.02 (d, *J* = 9.1 Hz, 1H), 4.14 (dt, *J* = 9.1, 2.7 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 163.0, 148.7, 148.4, 147.3, 138.0, 136.0, 131.2, 129.5, 129.1 (2C), 128.5 (2C), 128.3, 128.2, 127.8, 127.6, 126.7, 121.2, 81.4, 47.1; **IR** (film) 1731, 1620, 1592, 1567, 1491, 1454, 1415, 1375, 1266, 1241, 1158, 1045, 1031, 965 cm^{-1}; **HRMS** calcd for $C_{20}H_{14}ClNO_2Na$ ($M+Na^+$): 358.06053. Found: 358.06066.

(5*S,6*R**)-6-(3-Chloro-1-methyl-1*H*-pyrazol-4-yl)-5-phenyl-5,6-dihydro-2*H*-pyran-2-one (7e).**

A solution of diene **6e** (278 mg, 0.877 mmol, 1 equiv) and 2nd generation Hoveyda-Grubbs catalyst (16 mg, 26.3 µmol, 4 mol %) in toluene (5.0 mL) was heated at 100 °C. After 15 h, the solution was concentrated under reduced pressure and the crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:3 to 1:1) to afford lactone **7e** (164 mg, 65%) as a colorless oil. **R_f** = 0.33 (EtOAc/PE = 1:1); **IR** (film) 1720, 1562, 1494, 1413, 1376, 1264, 1223, 1179, 1057, 1014, 964, 913 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.35 (s, 1H), 7.32 – 7.25 (m, 3H), 7.11 – 7.06 (m, 2H), 6.94 (dd, *J* = 9.8, 2.5 Hz, 1H), 6.23 (dd, *J* = 9.8, 2.5 Hz, 1H), 5.37 (d, *J* = 10.3 Hz, 1H), 4.05 (dt^{app}, *J* = 10.3, 2.5 Hz, 1H), 3.78 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 163.4, 149.1, 137.6, 136.9, 131.0, 128.9 (2C), 128.3 (2C), 128.0, 121.0, 115.3, 77.0, 46.2, 39.6; **EI–MS** *m/z* (relative intensity) 244 (65), 209 (100), 194 (15), 168 (17), 167 (30), 166 (17), 165 (19), 153 (22), 142 (49), 141 (19), 140 (17), 139 (19), 131 (26), 129 (84), 76 (18); 65 (16), 63 (30), 51 (43), 50 (16); **HRMS** calcd for $C_{15}H_{13}ClN_2O_2Na$ ($M+Na^+$): 311.05578. Found: 311.05583.

4,6-Dichloro-5-((2*R,3*S**)-3-phenyl-3,6-dihydro-2*H*-pyran-2-yl)pyrimidine (5b).**

DIBAL-H (1M in hexane, 0.24 mL, 0.242 mmol, 1.2 equiv) was added to a solution of lactone **7b** (65 mg, 0.202 mmol, 1 equiv) in CH_2Cl_2 (0.89 mL) cooled at –78 °C. The solution was stirred at –78 °C and after 1 h was quenched with a saturated aqueous solution of Rochelle salt (2 mL). The mixture was stirred at rt until two limpid phases were obtained. The product was extracted with EtOAc (3 x 4 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to give the crude lactol. Et_3SiH (49 µL, 0.303 mmol, 1.5 equiv) and BF_3•Et_2O (26 µL, 0.202 mmol, 1 equiv) were added to a solution of the previously formed lactol in CH_2Cl_2 (0.89 mL) cooled at –78 °C. The solution was stirred at –78 °C and after 1 h a saturated aqueous solution of NH_4Cl (1 mL) was added and the product was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 6:94 to 12:88) to afford dihydropyran **5b** (24 mg, 39%) as a yellow oil. **R_f** = 0.49 (EtOAc/PE = 1:7); **IR** (film) 1538, 1514, 1492, 1453, 1414, 1369, 1330, 1216, 1138, 1104, 1051, 1025, 919 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.61 (s, 1H), 7.22 – 7.18 (m, 3H), 7.00 – 6.95 (m, 2H), 6.09 (dq^{app}, *J* = 10.3, 2.5 Hz, 1H), 6.00 (dq^{app}, *J* = 10.2, 2.0 Hz, 1H), 5.10 (d, *J* = 9.9 Hz, 1H), 4.46 – 4.44 (m, 2H), 4.36 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 162.0, 156.6 (2C), 138.8, 129.9, 128.6 (2C), 128.3 (2C), 128.0, 127.5, 126.6, 78.0, 66.4, 43.1; **EI–MS** *m/z* (relative intensity) 131 (10), 130 (100), 129 (48), 128 (15), 115 (27); **HRMS** calcd for $C_{15}H_{13}Cl_2N_2O_1$ ($M+H^+$): 307.03994. Found: 307.04030.

2-Chloro-3-((2*R,3*S**)-3-phenyl-3,6-dihydro-2*H*-pyran-2-yl)quinolone (5d).**

DIBAL-H (1M in hexane, 0.48 mL, 0.481 mmol, 1.2 equiv) was added to a solution of lactone **7d** (135 mg, 0.401 mmol, 1 equiv) in CH_2Cl_2 (1.8 mL) cooled at –78 °C. The solution was stirred at –78 °C and after 3 h, it was quenched with an aqueous solution of Rochelle salt (2 mL). The mixture was stirred at rt until two limpid phases were obtained. The product was extracted with EtOAc (3 x 4 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to give the crude lactol. Et_3SiH (97 µL, 0.602 mmol, 1.5 equiv) and BF_3•Et_2O (51 µL, 0.401 mmol, 1 equiv) were added to a solution of the previously formed lactol in CH_2Cl_2 (0.89 mL) cooled at –78 °C. The solution was stirred at –78 °C for 2 h. A second equivalent of BF_3•Et_2O (51 µL, 0.401 mmol, 1 equiv) was added and the solution was allowed to warm up to rt for 19 h. A saturated aqueous solution of NH_4Cl (1 mL) was then added and the product was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:3) to afford dihydropyran **5d** (69 mg, 50%) as a white solid. **mp** 138–141 °C; **R_f** = 0.16 (EtOAc/PE = 1:3); **IR** (film) 1620, 1591, 1561, 1489, 1409, 1383, 1326, 1203, 1176, 1130, 1108, 1049, 916 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.42 (s, 1H), 7.95 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.85 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.69 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.53 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.18 – 7.13 (m, 3H), 6.96 – 6.92 (m, 2H), 6.08 (m, 1H), 6.01 (dq^{app}, *J* = 10.2, 1.9 Hz, 1H), 5.02 (d, *J* = 9.2 Hz, 1H), 4.54 (dddd, *J* = 16.8, 4.0, 2.0,1.5 Hz, 1H), 4.43 (dq^{app}, *J* = 16.8, 2.6 Hz, 1H), 3.77 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 150.2, 146.9, 139.1, 137.5, 133.0, 130.4, 128.8, 128.5 (2C), 128.4 (2C), 128.2, 127.6, 127.2, 127.1, 126.9, 126.5, 78.1, 66.6, 49.0; **EI–MS** *m/z* (relative intensity) 131 (11), 130 (100) 129 (45), 128 (16), 127 (10), 115 (24); **HRMS** calcd for $C_{20}H_{17}ClNO$ ($M+H^+$): 322.09932. Found: 322.09933.

3-Chloro-1-methyl-4-((2*R,3*S**)-3-phenyl-3,6-dihydro-2*H*-pyran-2-yl)-1*H*-pyrazole (5e).**

DIBAL-H (1M in hexane, 0.93 mL, 0.931 mmol, 1.2 equiv) was added to a solution of lactone **7e** (224 mg, 0.776 mmol, 1 equiv) in CH_2Cl_2 (3.4 mL) cooled at –78 °C. The solution was stirred at –78 °C and after 2 h, it was quenched with an aqueous solution of Rochelle salt (3 mL). The mixture was stirred at rt until two limpid phases were obtained. The product was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to give the crude lactol. Et_3SiH (0.19 mL, 1.16 mmol, 1.5 equiv) and BF_3•Et_2O (0.01 mL, 0.776 mmol, 1 equiv) were added to a solution of the previously formed lactol in CH_2Cl_2 (3.4 mL) cooled at –78 °C. The solution was stirred and allowed to warm up to rt. After 22 h a saturated aqueous solution of NH_4Cl (3 mL) was added and the product was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:5 to 1:3) to afford dihydropyran **5e** (159 mg, 75%) as a slightly yellow oil. **R_f** = 0.27 (EtOAc/PE = 1:3); **IR** (film) 1563, 1492, 1443, 1407, 1328, 1241, 1179, 1094, 1075, 1051, 1026, 985 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.31 (s, 1H), 7.26 – 7.17 (m, 3H), 7.07 – 7.05 (m, 2H), 5.99 (m, 1H), 5.90 (dq^{app}, *J* = 10.3, 2.1 Hz, 1H), 4.47 – 4.40 (m, 1H), 4.44 (d, *J* = 8.9 Hz, 1H), 4.32 (m, 1H), 3.78 (s, 3H), 3.67 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* 140.5, 138.1, 130.2, 128.6, 128.4 (2C), 128.4 (2C), 126.8, 126.3, 118.2, 73.7, 65.9, 47.6, 39.5; **EI–MS** *m/z* (relative

intensity) 131 (11), 130 (100), 129 (62), 128 (19), 115 (34), 51 (12); **HRMS** calcd for $C_{15}H_{16}ClN_2O$ ($M+H^+$): 275.09457. Found: 275.09520.

1-(4-Fluorophenyl)-2-phenylbut-3-en-1-one.

Dess-Martin periodinane (176 mg, 0.415 mmol, 1.5 equiv) was added to a solution of alcohol **2a** (67 mg, 0.277 mmol, 1 equiv) in CH_2Cl_2 (2.3 mL) cooled at 0 °C and the solution was stirred at rt. After 2 h, the reaction mixture was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (2 mL). The product was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ (5 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 2:98 to 4:96) to afford the intermediate ketone (59 mg, 88%) as a colorless oil. $\mathbf{R_f}$ = 0.37 (EtOAc/PE = 4:96); **IR** (film) 1680, 1636, 1596, 1505, 1453, 1408, 1312, 1288, 1226, 1206, 1156, 1075, 988, 923 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 – 7.95 (m, 2H), 7.36 – 7.26 (m, 4H), 7.24 (m, 1H), 7.11 – 7.01 (m, 2H), 6.35 (ddd, *J* = 17.5, 10.1, 7.7 Hz, 1H), 5.24 – 5.20 (m, 2H), 5.09 (d, *J* = 17.3 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.8, 165.5 (d, *J* = 255.0 Hz), 138.1, 136.9, 132.6 (d, *J* = 3.1 Hz), 131.5 (d, *J* = 9.3 Hz, 2C), 129.0 (2C), 128.2 (2C), 127.2, 117.2, 115.6 (d, *J* = 21.9 Hz, 2C), 57.9; **EI–MS** *m/z* (relative intensity) 240 (0.7), 123 (100), 115 (12), 95 (30); **HRMS** the compound was not detected.

(1*S,2*S**)-1-(4-Fluorophenyl)-2-phenylbut-3-en-1-ol (*anti*-3a).**

L-Selectride (1M in THF, 0.73 mL, 0.730 mmol, 2 equiv) was added dropwise to a solution of the previously obtained ketone (87 mg, 0.364 mmol, 1 equiv) in THF (0.88 mL) cooled at –78 °C. The solution was stirred at –78 °C and, after 3 h, H_2O (0.01 mL) was added and the solution was warmed up to 0 °C. A 35% aqueous H_2O_2 solution (0.03 mL) was added and the solution was diluted with EtOAc (5 mL). The organic layer was washed with a saturated aqueous solution of $Na_2S_2O_3$ (2 mL), then with a saturated aqueous solution of $NaHCO_3$ (2 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (acetone/PE = 1:9 to 1:7) to afford alcohol *anti*-**3a** (70 mg, 79%) as a white solid. **mp** 61–63 °C; $\mathbf{R_f}$ = 0.31 (EtOAc/PE = 1:5); **IR** (film) 3429, 1637, 1603, 1510, 1453, 1380, 1223, 1157, 1044, 1013, 920 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H), 7.30 – 7.22 (m, 5H), 7.04 – 6.98 (m, 2H), 5.88 (ddd, *J* = 17.1, 10.3, 8.0 Hz, 1H), 5.00 (dt^{app}, *J* = 10.3, 1.5 Hz, 1H), 4.91 – 4.83 (m, 2H), 3.58 (t^{app}, *J* = 8.0 Hz, 1H), 1.95 (br s, 1H, OH); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.3 (d, *J* = 245.6 Hz), 140.0, 137.5 (d, *J* = 3.1 Hz), 137.3, 128.8 (2C), 128.7 (2C), 128.6 (d, *J* = 8.2 Hz, 2C), 127.2, 117.5, 114.9 (d, *J* = 21.2 Hz, 2C), 76.8, 58.7; **EI–MS** *m/z* (relative intensity) 125 (100), 118 (95), 117 (46), 115 (28), 97 (54), 95 (13), 91 (15), 77 (21); **HRMS** the compound was not detected.

1-((1*S,2*S**)-1-(Allyloxy)-2-phenylbut-3-en-1-yl)-4-fluorobenzene (*anti*-4a).**

NaH (60% in oil, 18 mg, 0.459 mmol, 1.55 equiv) was added to a solution of alcohol *anti*-**3a** (72 mg, 0.296 mmol, 1 equiv) in THF (1.1 mL) cooled at 0 °C. The solution was stirred at rt for 1 h, then allyl bromide (39 µL, 0.445 mmol, 1.5 equiv) was added. The solution was stirred at rt and after 39 h, H_2O (2 mL) was added and the product was extracted with Et_2O (3 × 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (CH_2Cl_2/pentane = 2:98 to 4:96) to afford ether *anti*-**4a** (60 mg, 72%) as a white solid. **mp** 37–39 °C; $\mathbf{R_f}$ = 0.19 (CH_2Cl_2/PE, 4:96); **IR** (film) 1639, 1603, 1509, 1453, 1419, 1221, 1156, 1076, 990, 920 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.24 – 7.09 (m, 5H), 7.01 – 6.94 (m, 2H), 5.93 (ddd, *J* = 17.0, 10.3, 8.2 Hz, 1H), 5.70 (ddt^{app}, *J* = 17.6, 10.5, 5.1 Hz, 1H), 5.11 – 5.03 (m, 2H), 4.96 (d, *J* = 10.4 Hz, 1H), 4.87 (d, *J* = 17.1 Hz, 1H), 4.55 (d, *J* = 7.4 Hz, 1H), 3.86 (br dd, *J* = 13.0, 4.2 Hz, 1H), 3.65 (dd, *J* = 13.2, 6.0 Hz, 1H), 3.59 (t^{app}, *J* = 7.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.3 (d, *J* = 245.2 Hz), 140.8, 138.1, 136.0 (d, *J* = 3.0 Hz), 134.6, 129.1 (d, *J* = 8.0 Hz, 2C), 128.8 (2C), 128.0 (2C), 126.4, 116.6, 116.5, 114.8 (d, *J* = 21.3 Hz, 2C), 83.4, 69.4, 57.3; **EI–MS** *m/z* (relative intensity) 165 (100), 123 (96), 117 (21), 115 (30), 91 (17); **HRMS** the compound was not detected.

(2*S,3*S**)-2-(4-Fluorophenyl)-3-phenyl-3,6-dihydro-2*H*-pyran (*cis*-5a).**

The 2nd generation Grubbs catalyst (1.4 mg, 1.68 µmol, 2 mol %) was added to a solution of diene *epi*-**4a** (24 mg, 83.9 µmol, 1 equiv) in degassed CH_2Cl_2 (0.45 mL). The solution was stirred at rt and after 23 h, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (CH_2Cl_2/pentane = 5:95 to 13:87) to afford dihydropyran *epi*-**5a** (17 mg, 79%) as a white solid. **mp** 71–73 °C; $\mathbf{R_f}$ = 0.64 (acetone/PE = 4:96); **GC** rt 6.503 min; **IR** (film) 1603, 1510, 1492, 1451, 1280, 1219, 1179, 1156, 1124, 1092, 1050 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.12 – 7.06 (m, 3H), 6.93 – 6.88 (m, 2H), 6.88 – 6.82 (m, 2H), 6.81 – 6.75 (m, 2H), 6.09 – 6.02 (m, 2H), 4.92 (d, *J* = 3.4 Hz, 1H), 4.60 – 4.46 (m, 2H), 3.42 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.6 (d, *J* = 244.6 Hz), 138.2, 136.2 (d, *J* = 3.2 Hz), 139.9 (2C), 127.9, 127.5 (d, *J* = 8.0 Hz, 2C), 127.4 (2C), 126.5, 126.4, 114.3 (d, *J* = 21.3 Hz, 2C), 78.6, 67.2, 47.4; **EI–MS** *m/z* (relative intensity) 254 (0.02), 131 (11), 130 (100), 129 (63), 128 (20), 115 (29); **HRMS** the compound was not detected.

(1*R,2*S**)-2-(4-Methoxyphenyl)-1-phenylbut-3-en-1-yl acrylate.**

(1*R**,2*S**)-2-(4-Methoxyphenyl)-1-phenylbut-3-en-1-yl acrylate was prepared according to **GP2** from alcohol **3j** (223 mg, 0.877 mmol). The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7) to afford the corresponding acrylate (186 mg, 69%) as a colorless oil. $\mathbf{R_f}$ = 0.47 (EtOAc/PE = 1:5); **IR** (film) 1721, 1611, 1511, 1403, 1247, 1177, 1035, 982 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.11 (m, 5H), 6.95 (br d, *J* = 8.5 Hz, 2H), 6.72 (br d, *J* = 8.5 Hz, 2H), 6.43 (dd, *J* = 17.3, 1.5 Hz, 1H), 6.20 – 6.08 (m, 2H), 6.05 (d, *J* = 8.5 Hz, 1H), 5.84 (dd, *J* = 10.4, 1.5 Hz, 1H), 5.15 – 5.06 (m, 2H), 3.77 – 3.71 (m, 1H), 3.73 (s, 3H) ; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.2, 158.2, 138.6, 137.6, 131.8, 130.9, 129.4 (2C), 128.6, 127.9 (2C), 127.7, 127.1 (2C), 117.0, 113.7 (2C), 78.4, 55.6, 55.1; **EI–MS** *m/z* (relative intensity) 236 (20), 148 (11), 147 (100), 115 (10), 91 (21), 55 (78); **HRMS** calcd for $C_{20}H_{20}O_3Na$ ($M+Na^+$): 331.13047. Found: 331.13036.

(5*S,6*R**)-5-(4-Methoxyphenyl)-6-phenyl-5,6-dihydro-2*H*-pyran-2-one (7j).**

A solution of the previously obtained acrylate (288 mg, 0.933 mmol, 1 equiv) and 2nd generation Hoveyda-Grubbs catalyst (18 mg, 30.0 µmol, 3 mol %) in toluene (5.3 mL) was heated at 100 °C. After 26 h, the solution was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:3) to afford lactone **7j** (246 mg, 94%) as a slightly brown solid. **mp** 123–125 °C; $\mathbf{R_f}$ = 0.38 (EtOAc/PE = 1:2); **IR** (film) 1726, 1611, 1512, 1455, 1375, 1303, 1249, 1178, 1157, 1056, 1031, 968 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.20 (m, 3H), 7.11 – 7.05 (m, 2H), 6.91 (dd, *J* = 9.8, 2.2 Hz, 1H), 6.82 (br d, *J* = 8.5 Hz, 2H), 6.75 (br d, *J* = 8.5 Hz, 2H), 6.23 (dd, *J* = 9.8, 2.6 Hz, 1H), 5.26 (d, *J* = 10.7 Hz, 1H), 3.84 (dt^{app}, *J* = 10.8, 2.5 Hz, 1H), 3.74 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 1637, 159.0, 149.6, 137.0, 129.5 (2C), 129.0, 128.4, 128.0 (2C), 127.0 (2C), 120.9, 114.0 (2C), 86.0 55.1, 47.0; **EI–MS** *m/z* (relative intensity) 280 (0.10), 174 (100), 159 (20), 131 (39), 103 (28), 77 (21); **HRMS** calcd for $C_{18}H_{17}O_3$ ($M+H^+$): 281.11722. Found: 281.11722.

(5*S,6*R**)-5-(4-Methoxyphenyl)-6-phenyltetrahydro-2*H*-pyran-2-one (8).**

Wilkinson catalyst (13 mg, 13.7 µmol, 2.5 mol %) was added to a solution of lactone **7j** (154 mg, 0.549 mmol, 1 equiv) in toluene (6.4 mL). The solution was purged with H_2 and stirred at rt, and after 24 h, a second portion of Wilkinson catalyst (13 mg, 13.7 µmol, 2.5 mol %) was added. The solution was stirred for 3 days. The reaction was filtered through a pad of Celite and concentrated under reduced pressure. The crude

product was purified by flash chromatography on silica gel (EtOAc/PE = 1:3 to 1:2) to afford lactone **8** (132 mg, 85%) as a white solid. **mp** 111–113 °C; $\mathbf{R_f}$ = 0.30 (EtOAc/PE = 1:2); **IR** (film) 1730, 1512, 1455, 1348, 1331, 1275, 1247, 1194, 1180, 1061, 1029, 987 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 – 7.16 (m, 3H), 7.05 – 7.00 (m, 2H), 6.87 (d^{app}, J = 8.9 Hz, 2H), 6.72 (d^{app}, J = 8.9 Hz, 2H), 5.29 (d, J = 10.3 Hz, 1H), 3.71 (s, 3H), 3.02 (ddd, J = 11.0, 10.3, 4.7 Hz, 1H), 2.88 (ddd, J = 17.9, 6.4, 4.4 Hz, 1H), 2.74 (ddd, J = 17.8, 10.1, 6.9 Hz, 1H), 2.28 (dddd, J = 13.9, 11.0, 10.0, 6.5, Hz, 1H), 2.16 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.8, 158.5, 138.2, 131.3, 128.7 (2C), 128.1, 128.0 (2C), 126.7 (2C), 113.8 (2C), 87.1, 55.0, 46.4, 30.0, 27.0; **EI–MS** *m/z* (relative intensity) 282 (3), 176 (20), 135 (10), 134 (100); **HRMS** calcd for $C_{18}H_{19}O_3$ ($M+H^+$): 283.13257. Found: 283.13298.

(5*S,6*R**)-2-(1,3-Dithian-2-yl)-5-(4-methoxyphenyl)-6-phenyltetrahydro-2*H*-pyran-2-ol.**

n-BuLi (2.2M, 0.19 mL, 0.426 mmol, 1.1 equiv) was added to a solution of 1,3-dithiane (51 mg, 0.426 mmol, 1.1 equiv) in THF (1.9 mL) cooled at –78 °C. The solution was stirred at –78 °C, and after 15 min a solution of lactone **8** (109 mg, 0.387 mmol, 1 equiv) in THF (1.4 mL) was added. The solution was stirred at 0 °C and after 2.5 h, a saturated aqueous solution of NH_4Cl (2 mL) was added and the product was extracted with Et_2O (3 × 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:7 to 1:5) to afford an intermediate lactol (83 mg, 53%) as a white solid. **mp** 154–157 °C; $\mathbf{R_f}$ = 0.19 (EtOAc/PE = 1:5); **IR** (film) 3437, 1611, 1512, 1452, 1386, 1246, 1136, 1113, 1060, 1035, 993, 970 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 – 7.09 (m, 5H), 6.90 (br d, J = 8.6 Hz, 2H), 6.67 (br d, J = 8.6 Hz, 2H), 5.00 (d, J = 10.6 Hz, 1H), 4.19 (d, J = 2.6 Hz, 1H, OH), 3.70 (s, 3H), 3.53 (s, 1H), 3.44 (m, 1H), 3.05 (m, 1H), 2.82 (ddd, J = 12.9, 10.8, 4.1 Hz, 1H), 2.66 (tdd^{app}, J = 13.3, 4.6, 2.6 Hz, 1H), 2.51 (dt^{app}, J = 13.3, 4.4 Hz, 1H), 2.40 (m, 1H), 2.30 (dt^{app}, J = 13.3, 4.4 Hz, 1H), 2.01 – 1.89 (m, 3H), 1.72 (ddd, J = 12.9, 4.2, 2.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.9, 140.8, 134.0, 128.9 (2C), 127.7 (2C), 127.5 (2C), 127.2, 113.4 (2C), 99.8, 78.9, 55.0, 50.3, 48.3, 31.1, 27.8, 26.5, 26.0, 24.8; **EI–MS** *m/z* (relative intensity) 176 (18), 135 (11), 134 (100); **HRMS** calcd for $C_{22}H_{26}O_3S_2Na$ ($M+Na^+$): 425.12156. Found: 425.12164.

(2*R,3*S**,6*S**)-6-(1,3-Dithian-2-yl)-3-(4-methoxyphenyl)-2-phenyltetrahydro-2*H*-pyran (9).**

Et_3SiH (0.13 mL, 0.774 mmol, 5 equiv) and BF_3•Et_2O (78 µL, 0.619 mmol, 4 equiv) were added to a solution of the previously obtained lactol (62 mg, 0.155 mmol, 1 equiv) in CH_2Cl_2 (2 mL) cooled at –78 °C. The solution was stirred at –78 °C for 1 h and then it was slowly allowed to warm up to rt. After 12 h a saturated aqueous solution of $NaHCO_3$ (0.5 mL) was added to the reaction mixture that was concentrated under reduced pressure. CH_2Cl_2 (5 mL) was added and the organic layer was washed with H_2O (2 mL), brine (2 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/PE = 1:5) to afford tetrehydropyran **9** (30 mg, 50%) as a white solid. **mp** 143–145 °C; $\mathbf{R_f}$ = 0.45 (EtOAc/PE = 1:5); **IR** (film) 1611, 1512, 1453, 1276, 1244, 1178, 1105, 1066, 1034, 907 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.15 – 7.09 (m, 3H), 7.05 – 7.01 (m, 2H), 6.82 (br d, J = 8.6 Hz, 2H), 6.66 (br d, J = 8.6 Hz, 2H), 4.40 (d, J = 10.1 Hz, 1H), 4.29 (d, J = 4.8 Hz, 1H), 3.92 (ddd, J = 10.8, 4.8, 2.3 Hz, 1H), 3.71 (s, 3H), 2.99 – 2.89 (m, 2H), 2.89 – 2.79 (m, 2H), 2.69 (m, 1H), 2.16 – 2.05 (m, 2H), 2.03 – 1.87 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.9, 140.7, 133.8, 128.8 (2C), 127.7 (2C), 127.1, 127.0 (2C), 113.4 (2C), 85.9, 80.7, 55.0, 51.7, 49.1, 31.6, 30.1, 29.9, 28.9, 26.2; **EI–MS** *m/z* (relative intensity) 386 (5), 173 (10), 134 (52), 121 (19), 119 (100), 91 (16); **HRMS** calcd for $C_{22}H_{26}O_2S_2Na$ ($M+Na^+$): 409.12664. Found: 409.12682.

((2*S,5*S**,6*R**)-5-(4-Methoxyphenyl)-6-phenyltetrahydro-2*H*-pyran-2-yl)methanol (11).**

MeI (85 µL, 0.137 mmol, 2 equiv) and Na_2CO_3 (8.7 mg, 82.0 µmol, 1.2 equiv) were added to a solution of dithiane **9** (26 mg, 68.3 µmol, 1equiv) in a mixture of acetone/H_2O (9:1, 8.6 mL). The solution was heated at 35 °C and after 26 h it was concentrated under reduced pressure. EtOAc (5 mL) and H_2O (2 mL) were then added, and the mixture vigorously stirred. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give a crude aldehyde **10**. $NaBH_4$ (5.2 mg, 0.137 mmol, 2 equiv) was added to a solution of aldehyde **10** in a cooled (0 °C) mixture of Et_2O/MeOH (1:1, 0.76 mL). The solution was stirred at rt and after 4 h, acetone (1 mL) was added and the solution was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (acetone/pentane = 1:5 to 1:3) to afford alcohol **11** (12 mg, 57%) as a colorless oil. $\mathbf{R_f}$ = 0.33 (EtOAc/PE, 1:3); **GC** rt 8.164 min; **IR** (film) 3430, 1611, 1583, 1512, 1454 1265, 1244, 1178, 1111, 1069, 1037 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.18 – 7.12 (m, 3H), 7.07 – 7.02 (m, 2H), 6.84 (d^{app}, J = 8.4 Hz, 2H), 6.67 (d^{app}, J = 8.4 Hz, 2H), 4.39 (d, J = 10.1 Hz, 1H), 3.77 (m, 1H), 3.71 (s, 3H), 3.70 – 3.60 (m, 2H), 2.71 (ddd, J = 12.1, 10.1, 3.9 Hz, 1H), 2.22 (br s, 1H, OH), 2.10 (dq^{app}, J = 13.4, 4.3 Hz, 1H), 1.99 (qd^{app}, J = 12.9, 4.1 Hz, 1H), 1.74 (ddt^{app}, J = 13.2, 4.1, 2.6 Hz, 1H), 1.63 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.9, 140.9, 134.0, 128.9 (2C), 127.7 (2C), 127.3, 127.2 (2C), 113.5 (2C), 85.4, 78.5, 66.2, 55.0, 49.2, 31.5, 27.6; **EI–MS** *m/z* (relative intensity) 298 (6), 147 (15), 135 (10), 134 (100), 119 (11), 91 (17); **HRMS** calcd for $C_{19}H_{22}O_3Na$ ($M+Na^+$): 321.14612. Found: 321.14606.

Acknowledgements

Janssen Pharmaceutica is thanked for financial support.

Keywords: dihydropyrans • tetrahydropyrans • heterocycles • allylboration • ring-closing metathesis

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