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Iron-Catalyzed Synthesis of C2 Aryl- and *N*-Heteroaryl-Substituted Tetrahydropyrans

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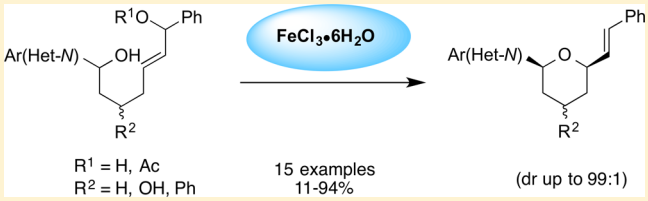
Supporting Information

ABSTRACT: An iron-catalyzed cyclization of hydroxy allylic derivatives into tetrahydropyrans possessing an *N*-heteroaryl at C2 is disclosed. The reaction proceeds with good yield and in high diastereoselectivity in favor of the more stable isomer. The diastereoselectivity results from an iron-induced reopening of the tetrahydropyrans, allowing a thermodynamic equilibration. The method allows access to a variety of 2,6-disubstituted as well as 2,4,6-trisubstituted tetrahydropyrans that could be considered as attractive scaffolds for the pharmaceutical industry.



INTRODUCTION

Substituted tetrahydropyrans (THPs) are ubiquitous motifs in natural and non-natural biologically active products, and some examples are depicted in Figure 1.[1] Among them, 2-aryl/heteroaryl THPs exhibit a wide range of biological properties, including cytotoxicity, tumor growth inhibition, and inhibition of tyrosine kinase and dipeptidyl peptidase 4, which is involved in type 2 diabetes.[2]

Because of their potent pharmacological properties, a myriad of synthetic methods has been developed for the construction of THP rings.[3] Among the existing methods, the metal-catalyzed cyclization of hydroxy allylic alcohols of type **A** emerged as an efficient and stereoselective strategy to access THPs of type **B**. In addition, as water is the only byproduct, this reaction meets the current environmental requirements that encourage the development of eco-friendly and atom-economic processes (Scheme 1).

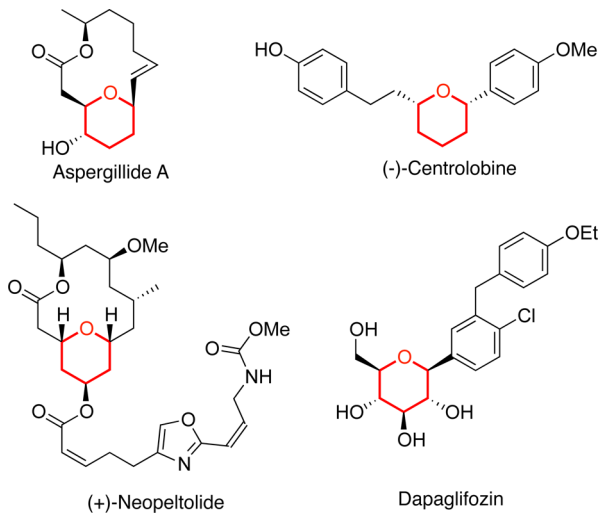
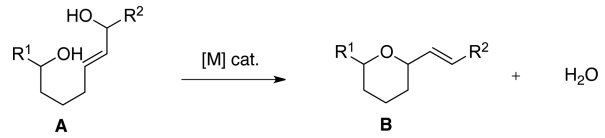


Figure 1. Tetrahydropyran units in biologically active natural products.

Scheme 1. Metal-Catalyzed Cyclization of Monoallylic Diols



For a long time, Pd(II)-catalysis ruled the field of metal-catalyzed heterocyclizations, and a large array of substituted THPs has been formed through intramolecular oxypalladation. A 1,3-chirality transfer was responsible for the high diastereoselectivity of the reaction (Scheme 2).[4]

A few years later, Au(I)-catalyzed cyclizations of hydroxy allylic alcohols, processing through an S_N2' pathway, were developed, delivering THPs in good yields and stereoselectivities. A 1,3-chirality transfer is the key to account for the high stereoselectivity, and enantiomers can be obtained by switching the geometry of the double bond (Scheme 3).[5]

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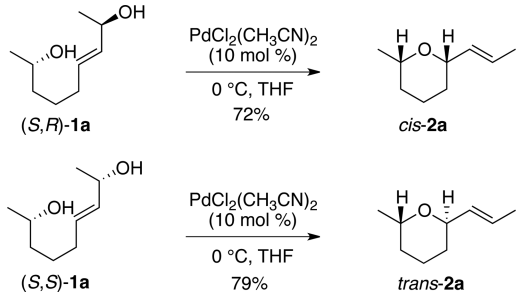
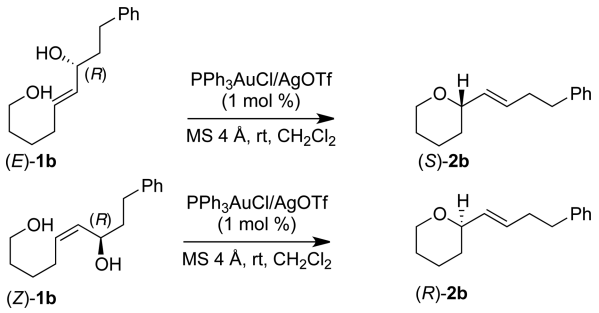
Scheme 2. Pd(II)-Catalyzed Synthesis of Tetrahydropyrans



Scheme 3. Au-Catalyzed Synthesis of Tetrahydropyrans

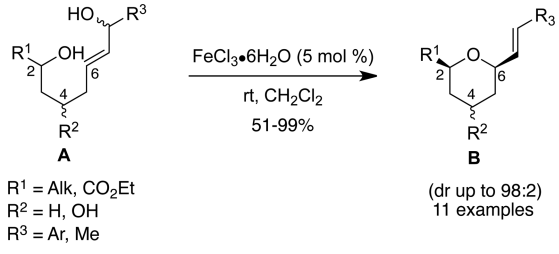


Despite their recognized utility, palladium and gold catalysis have some drawbacks, such as high costs, limited supply, and toxicity.[6,7] Furthermore, only a few examples of metal-catalyzed heterocyclizations of hydroxy allylic and/or benzylic alcohols delivering 2-aryl THPs have been reported to date,[8,9] and to the best of our knowledge, the preparation of 2-*N*-heteroaryl THPs using this cyclization strategy has not yet been described, which may be due to the Lewis basicity of *N*-heteroaromatics that could poison the metal catalyst.[10]

During the past decade, a growing interest has been devoted to iron catalysis.[11] Besides being cheap and presenting low toxicity, iron salts exhibit attractive chemical properties, including the ability to activate allylic and/or benzylic alcohols.[12] In 2010, we reported the highly diastereoselective $FeCl_3$-catalyzed formation of 2,6-disubstituted THPs.[13] This method was extended to the synthesis of a wide variety of THP units, including 2,4,6-trisubstituted THPs, but was restricted so far to alkyl, ester, alkenyl, or hydroxyl C2 and C4 substituents (Scheme 4).[14,15]

In this study, we focused on the preparation of 2-aryl and 2-*N*-heteroaryl THPs, and a full account of our results is reported herein.

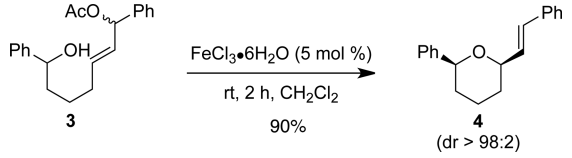
Scheme 4. Iron-Catalyzed Synthesis of 2,6- and 2,4,6-Substituted THPs



RESULTS AND DISCUSSION

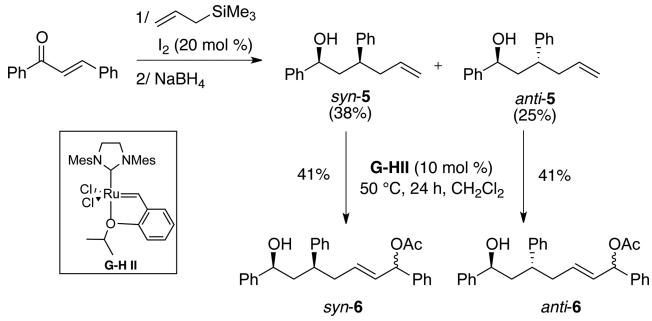
Synthesis of C2 Aryl-Tetrahydropyrans. On the basis of our previous results obtained for the formation of 2,6-disubstituted THPs possessing an alkyl substituent at C2, we decided to treat hydroxy acetate **3** with a catalytic amount of $FeCl_3{\cdot}6H_2O$ (5 mol %).[16] The presence of a benzylic alcohol and a benzylic acetate in the starting material was first envisioned as a potential difficulty, but pleasingly, the cyclization of hydroxy acetate **3** proceeded smoothly, furnishing THP **4** as a single *cis*-diastereomer in good yield (90%) (Scheme 5).

Scheme 5. Synthesis of a C2-Ar Tetrahydropyran



The method also allowed access to 2,4,6-trisubstituted THPs. For the introduction of a phenyl group at the C4 position, a Sakurai allylation was performed on (*E*)-chalcone, and the corresponding ketone was reduced to give a mixture of diastereomeric alcohols *syn*-**5** and *anti*-**5**, which were separated by flash chromatography on silica gel. A cross-metathesis of *syn*-**5** and *anti*-**5** with 1-phenylallyl acetate in the presence of the second generation Grubbs–Hoveyda catalyst **G-HII** furnished allylic acetates *syn*-**6** and *anti*-**6**, respectively, in 41% yield in both cases (Scheme 6).

Scheme 6. Preparation of Allylic Acetates *syn*-6 and *anti*-6



When *anti*-**6** was treated with $FeCl_3{\cdot}6H_2O$ (5 mol %), the corresponding *cis*-2,4,6-trisubstituted THP **7a** was isolated as a single diastereomer with a good yield of 82% after only 1 h at rt. By contrast, *syn*-**6** led to a mixture of THPs **7b** and **7c** (65%) with poor diastereoselectivity after 48 h. This result may be explained by a small difference of stability between THPs **7b** and **7c**, as both THPs possess one of the three substituents in an axial position. Prolonged heating of the mixture of **7b** and **7c** at 50 °C in the presence of $FeCl_3{\cdot}6H_2O$ exclusively led to ketone **8**, which might result from a 1,5-hydride shift (Scheme 7).

We also studied the influence of a hydroxyl group at C4 on the outcome of the cyclization. A mixture of *cis*- and *trans*-acetonides **9** was obtained in 5 steps from benzaldehyde, and then, treatment with an aqueous 2 M solution of HCl (5 mol %) led to diol *anti*-**10** and to untouched acetonide *cis*-**9**.[17,18] After separation, *cis*-**9** was cleaved into the corresponding *syn*-diol using 5 equiv of aq 1 M HCl (83%) (Scheme 8).

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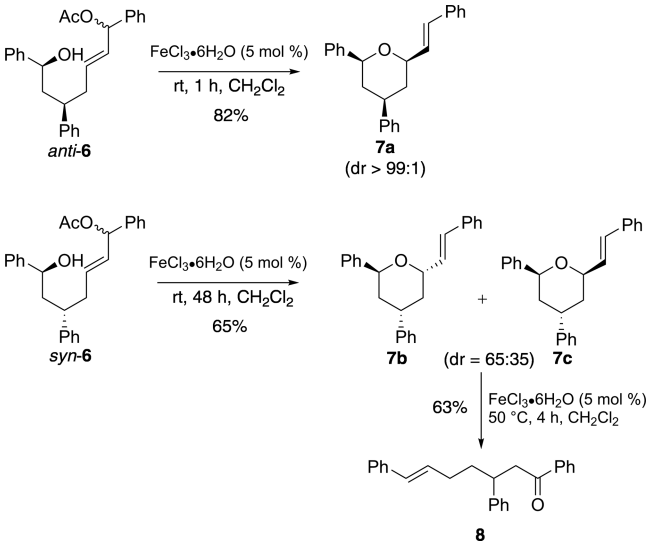
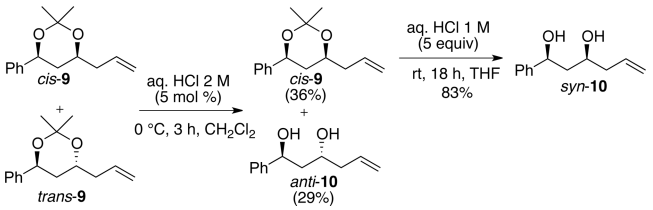
Scheme 7. Access to Trisubstituted THPs 12a−12c

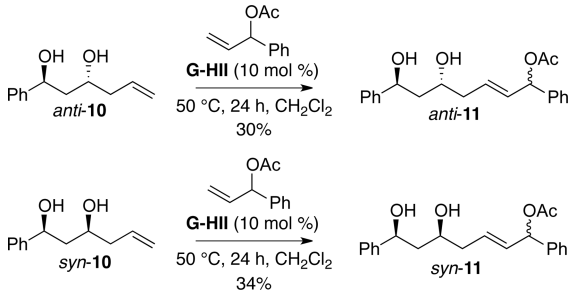


Scheme 8. Preparation of Diols *syn*-10 and *anti*-10



Both diols *anti*-**10** and *syn*-**10** were involved in a cross-metathesis with 1-phenylallyl acetate, and the corresponding allylic acetates *anti*-**11** and *syn*-**11** were isolated in moderate yields (30 and 34%, respectively) (Scheme 9).

Scheme 9. Synthesis of Allylic Acetates *anti*-11 and *syn*-11

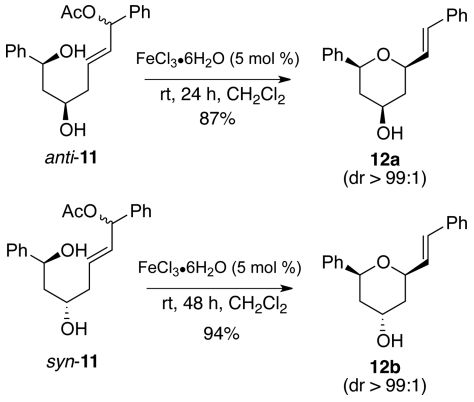


Pleasingly, upon treatment with $FeCl_3 \cdot 6H_2O$ (5 mol %), allylic acetates *anti*-**11** and *syn*-**11** delivered the expected THPs **12a** and **12b**, respectively, in excellent yields and diastereomeric ratios (dr >99:1) (Scheme 10).

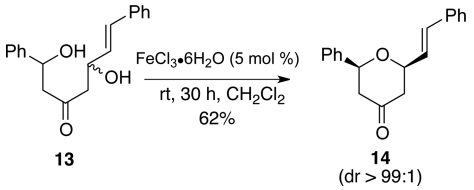
Finally, *cis*-tetrahydropyranone **14** was prepared through the iron-catalyzed cyclization of diol **13**.[19] The moderate yield of 62% could be explained by a partial degradation of the product during the reaction (Scheme 11). It should be mentioned that no formation of a dienone resulting from a dehydration process was observed during the reaction.

Synthesis of C2-Heteroaryl-Tetrahydropyrans. Encouraged by these positive results, we then turned our attention toward the synthesis of THPs incorporating heteroaryl moieties that could possess the ability of modulating pharmacological

Scheme 10. Formation of 2,4,6-Trisubstituted THPs 12a and 12b

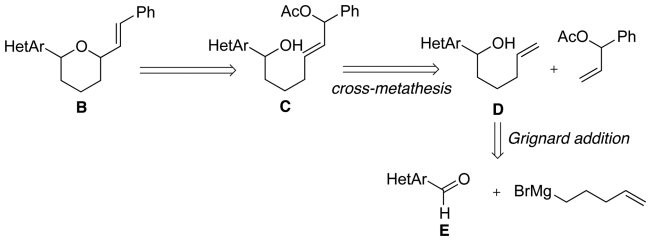


Scheme 11. Synthesis of a 2,6-Disubstituted Tetrahydropyranone



properties. To access the precursor of cyclization **C**, we planned a cross-metathesis between unsaturated alcohols **D** and 1-phenylallyl acetate. Alcohols **D** would result from the addition of the Grignard reagent derived from 1-bromopent-4-ene on a variety of aldehydes **E** (Scheme 12).

Scheme 12. Retrosynthesis of Precursors of Hydroxy Allylic Acetates B



Initially, the introduction of a pyridyl substituent was examined, and alcohol **16a** was obtained by the addition of the Grignard reagent prepared from 1-bromopent-4-ene on nicotinaldehyde **15a**. Disappointingly, when **16a** was suggested to the cross-metathesis conditions in the presence of 1-phenylallyl acetate and Grubbs−Hoveyda second-generation catalyst (**G-HII**), no reaction occurred. We hypothesized that the presence of the basic nitrogen on the pyridine poisoned the ruthenium catalyst, thus preventing the reaction from proceeding. To overcome this difficulty, we recently showed that the introduction of an electron-withdrawing group on the pyridyl moiety restored the reactivity of the substrate in the cross-metathesis by reducing the Lewis and/or Brønsted basicity of the nitrogen atom of the *N*-heteroaryl group.[20] As a consequence, a chlorine atom was introduced on the pyridyl ring, and the cross-metathesis between alcohol **16b** and 1-phenylallyl acetate furnished desired hydroxy allylic acetate **17b** in a satisfactory yield of 55% (Scheme 13).[15]

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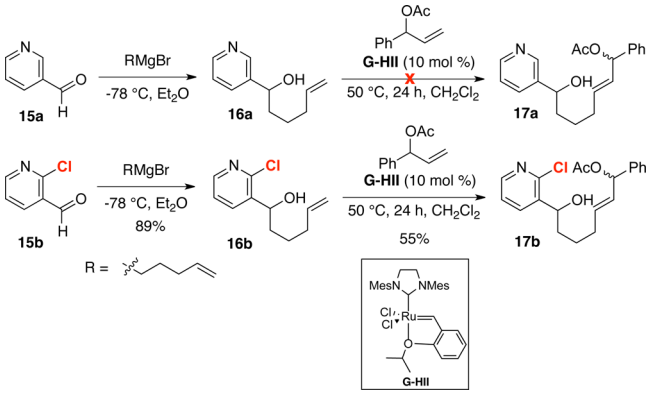
Scheme 13. Cross-Metathesis Involving Pyridine-Containing Alkenes



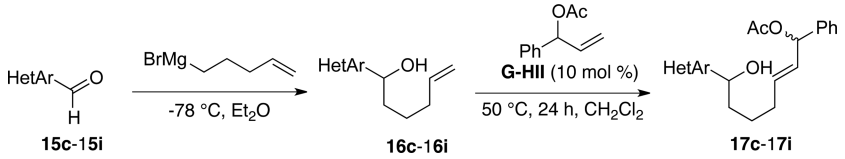
The same sequence of reactions was then applied to a wide range of heteroaromatic aldehydes **15c−15i** (Table 1). The cross-metathesis tolerated the presence of chloro-pyrimidines, -(iso)quinolines, -pyrazoles, -imidazoles, -indoles, and -pyrroles, and in all cases, the expected products were formed in moderate but acceptable yields ranging from 46 to 60% (Table 1).[15,21]

With the hydroxy allylic acetate derivatives in hand, the key cyclization step was examined next (Table 2). Gratifyingly, when **17b**, incorporating a 2-chloro-pyridyl group, was treated with 5 mol % of $FeCl_3{\cdot}6H_2O$, the corresponding disubstituted THP **18b** was isolated in good yield (81%) as a single *cis*-isomer. Even if the complete conversion of the starting material was obtained after 2 h, a long reaction time (120 h) was necessary to reach the high diastereoselectivity in favor of the *cis* isomer. Indeed, by monitoring the reaction using GC/MS, an evolution of the diastereomeric ratio from 66:34 to 99:1 was noted (Table 2, entries 1−4).

This observation suggests an iron-induced reopening of the *cis*- and *trans*-THPs that proceeds via zwitterionic intermediate **F** (Scheme 14). Because of this equilibration, thermodynamic control can be invoked to explain the formation of the more stable *cis* isomer as the major compound. Compared to our previous results[13,14] (see Scheme 5), the isomerization needed a longer reaction time in the presence of *N*-heteroaromatic substituents than with alkyl substituents, and we hypothesized that, despite the chlorine substituent, the nitrogen atom could coordinate the iron catalyst, thus slowing the equilibration process between the *cis*- and *trans*-THPs.[22−24]

The reaction was then extended to the synthesis of 2,6-disubstituted THPs bearing a range of *N*-heteroaromatic substituents at C2. The cyclization proceeded smoothly in

Table 1. Synthesis of Allylic Acetates 17c−17i



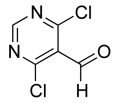
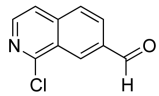
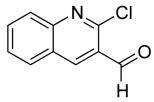
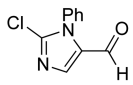
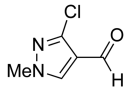
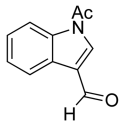
entry	**15**		**16** (yield %)	**17** (yield %)
1	**15c**		**16c** (29%)	**17c** (60%)
2	**15d**		**16d** (83%)	**17d** (49%)
3	**15e**		**16e** (46%)	**17e** (52%)
4	**15f**		**16f** (78%)	**17f** (51%)
5	**15g**		**16g** (95%)	**17g** (46%)
6	**15h**		**16h** (48%)	**17h** (46%)
7	**15i**		**16i** (61%)	**17i** (55%)

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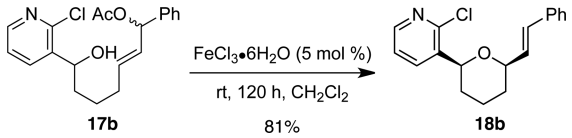
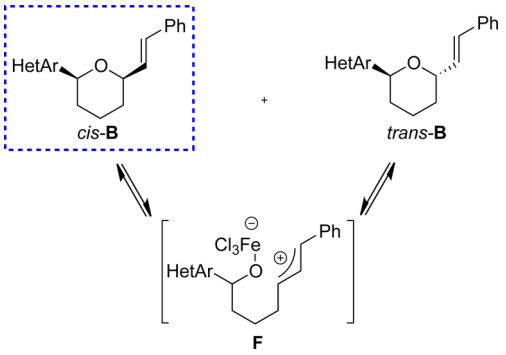
Table 2. Cyclization of Hydroxyl Acetate 17b



entry	time	*cis*/*trans*
1	3 h	66:34
2	7 h	73:27
3	24 h	81:19
4	120 h	99:1

Scheme 14. $FeCl_3$-Induced Reopening of 2,6-Disubstituted THPs



the presence of a chloro-pyrimidine or chloro-(iso)-quinolines (Table 3, entries 1−3). Upon treatment with $FeCl_3·6H_2O$, **17f** was transformed into THP **18f** bearing a chloro-imidazole moiety with a moderate yield (57%) after 18 days (Table 3, entry 4). Once again, the long reaction time was due to difficulties in reaching a high diastereoselectivity. THPs **18g** and **18h** that possess a pyrazole and an indole at the C2 position, respectively, were synthesized in good yields and excellent diastereomeric ratios (Table 3, entries 5−6). In contrast, the reaction conditions were not compatible with a pyrrole group as the corresponding THP **18i** was obtained with a low yield of 11%, probably due to the degradation of the starting material in the presence of the iron catalyst (Table 3, entry 7).

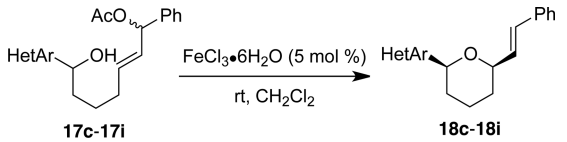
Worthy of note is that the *N*-heteroaryl group could be introduced at the allylic position (R^2 substituent) through a cross-metathesis between alcohol **16j** and allylic acetate **19** (29%). When **17j** was treated with $FeCl_3·6H_2O$, cyclized product **18j** was isolated as a single *cis* isomer with a good yield (72%). Gratifyingly, this cyclization method was compatible with sophisticated heterocycles, such as pyrrolo-pyrimidine (Scheme 15).

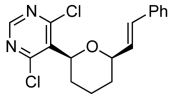
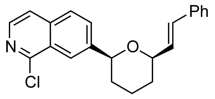
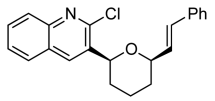
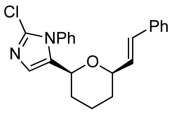
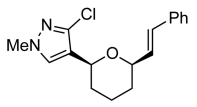
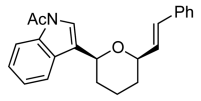
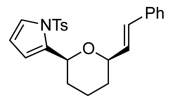
The presence of the vinylic substituent at C6 on the THPs offers the opportunity for further transformations. A dihydroxylation was performed on THP **18b**, furnishing diol **20** in a 2:1 diastereomeric ratio.[25] A subsequent oxidative cleavage delivered aldehyde **21**, which was successfully reduced to alcohol **22** (Scheme 16). The latter could be engaged in further transformations to obtain a variety of functionalized compounds.

CONCLUSIONS

A chemo- and diastereoselective iron-catalyzed cyclization was developed to access a wide variety of tetrahydropyrans possessing an *N*-heteroaryl at C2, which are attractive scaffolds

Table 3. Formation of 2-HetAr THPs 18c−18i



entry	17	time	18 (yield)[a]
1	**17c**	5 d	 **18c** (91%)
2	**17d**	5 d	 **18d** (83%)
3	**17e**	5 d	 **18e** (76)%
4	**17f**	18 d	 **18f** (57%)
5	**17g**	2 d	 **18g** (64%)
6	**17h**	2 h	 **18h** (56%)
7	**17i**	45 min	 **18i** (11%)

[a]All the THPs were obtained as a single *cis*-diastereomer.

for the pharmaceutical industry. The cyclization proceeded in good yields and with excellent diastereoselectivities in favor of the *cis*-THP. The use of the cheap and low-toxicity $FeCl_3·6H_2O$ as the catalyst as well as the small amount of waste produced during the process makes this method interesting for industrial purposes. The double bond can be submitted to further transformations, and thus, this cyclization method could be useful to prepare valuable functionalized compounds.

EXPERIMENTAL SECTION

General Experimental Methods. All moisture and oxygen sensitive reactions were carried out in oven-dried glassware under an argon atmosphere. THF, Et_2O, and CH_2Cl_2 were dried using a purificator. Acetone, petroleum ether (PE), pentane, and ethyl acetate (EtOAc) were used as received. Commercially available reagents were used as received. Reactions run at room temperature were performed between 20 and 25 °C. Solvent evaporations were conducted under reduced pressure at temperatures less than 45 °C. TLC was performed on silica gel plates visualized either with a UV lamp (254 nm) or using a staining solution (*p*-anisaldehyde or $KMnO_4$) followed by heating. Column chromatography was carried out under positive pressure using silica gel (Merck-Kieselgel 60, 230−400) and the indicated solvents [v/v; used without purification, including petroleum ether (boiling range 40−60 °C)]. ^1H NMR spectra of samples were run at 400 MHz, and chemical shifts are given in ppm (δ) comparatively to the residual solvent signal, which was used as an internal reference (acetone-d_6: δ =

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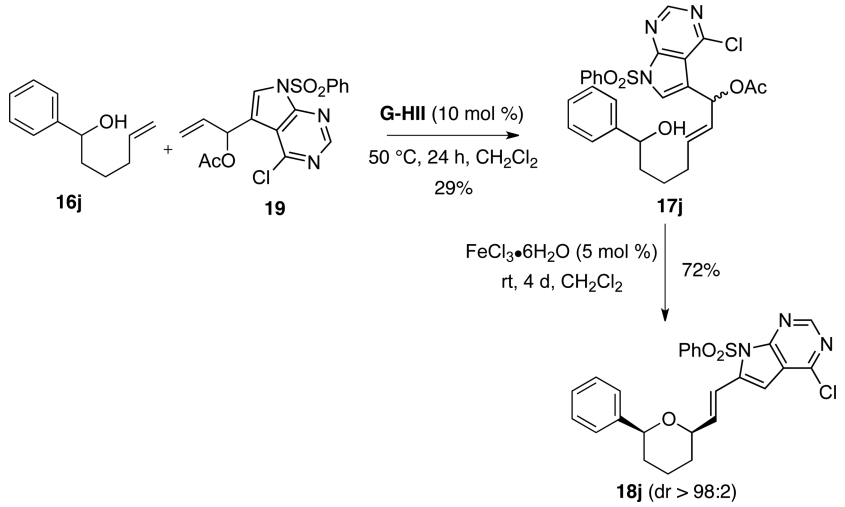
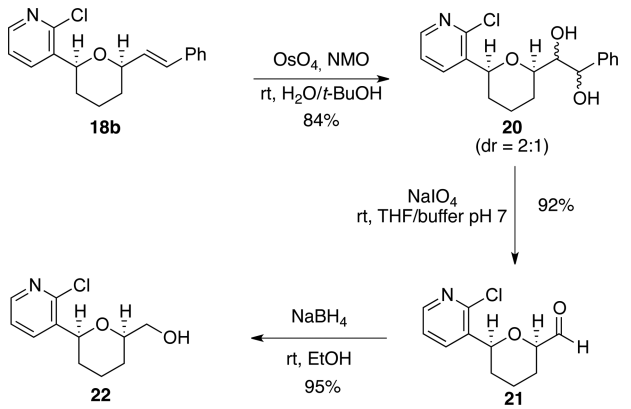
Scheme 15. Synthesis of THP Incorporating a Pyrrolo-Pyrimidine Motif



Scheme 16. Functionalization of the Double Bond



2.05 ppm; $CDCl_3$: δ = 7.26 ppm). Coupling constants (J) are given in Hertz (Hz), and the following abbreviations are used to describe the signal multiplicity: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quadruplet), quint (quintuplet), and m (multiplet). ^{13}C NMR spectra of the samples were run at 100 MHz. Chemical shifts are given in ppm (δ) comparatively to the residual solvent signal, which was used as an internal reference (acetone-d_6: δ = 29.84 ppm; $CDCl_3$: δ = 77.16 ppm). Infrared (IR) spectra were recorded neat (IRFT), and wavenumbers are indicated in cm^{-1}. Low-resolution mass spectra with electronic impact (MS-EI) were recorded on a gas chromatograph−mass spectrometer. High-resolution mass spectra (HRMS) were performed using ESI and a TOF mass analyzer.

*1-Chloroisoquinoline-7-carbaldehyde (**15d**).* To a stirred solution of 7-bromo-1-chloroisoquinoline (790 mg, 3.26 mmol, 1.0 equiv) in dry THF (32 mL) at −78 °C was slowly added a solution of *n*-BuLi (2.5 M hexanes, 1.37 mL, 3.42 mmol, 1.05 equiv), and the resulting mixture was stirred at −78 °C for 40 min. Methylformate (0.606 mL, 9.77 mmol, 3 equiv) was added dropwise, and the solution was stirred at −78 °C for 1 h and then at rt for another 1 h. The reaction was quenched with ice, and a saturated aqueous solution of NH_4Cl (20 mL) was added to the reaction mixture. The phases were separated and the aqueous layer was extracted with EtOAc (2 × 20 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give an orange solid, which was purified by column chromatography (PE/EtOAc = 4:1) to furnish pure aldehyde **15d** (398 mg, 64%) as white crystals. These data are in full accordance with those reported in the literature.[26] R_f = 0.42 (PE/EtOAc = 3:1); mp 143−145 °C; IR (neat) 2871, 1690, 1624, 1549, 1304, 1253, 1224, 1192, 1159, 1135 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.18 (d, J = 0.8 Hz, 1H), 8.73 (dt_{app}, J = 1.6 and 0.8 Hz, 1H), 8.36 (d, J = 5.6 Hz, 1H), 8.17 (dd, J = 8.8 and 1.6 Hz, 1H), 7.91 (bd, J = 8.4 Hz, 1H), 7.63 (dd, J = 5.6 and 0.8 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 191.0, 153.0, 144.5, 140.8, 136.1, 132.3, 128.4, 128.0, 126.6, 120.8; LRMS (EI) m/z (rel intensity) 193 ($[M]^{\cdot+}$, 31), 191 ($[M]^{\cdot+}$, 100), 190 (92), 164 ($[M - CHO]^+$, 19), 162 ($[M - CHO]^+$, 55), 128 (21), 127 ($[M - Cl - CHO]^{\cdot+}$, 28), 126 (23), 101 (19), 100 (20), 99 (21), 75 (31), 74 (20), 51 (29), 50 (24).

*2-Chloroquinoline-3-carbaldehyde (**15e**).* To an ice-cold stirred solution of diisopropylamine (363 μL, 2.57 mmol, 1.2 equiv) in dry THF (6 mL) was added dropwise *n*-BuLi (2.5 M in hexanes, 941 μL, 2.35 mmol, 1.1 equiv), and the mixture was stirred at 0 °C for 20 min. The reaction was then cooled to −78 °C. 2-Chloroquinoline (350 mg, 2.14 mmol, 1.0 equiv) was added neat, and the resulting mixture was stirred at −78 °C for 35 min. DMF (273 μL, 3.53 mmol, 1.65 equiv) was slowly added, and the solution was stirred at −78 °C for 30 min and then at rt for 1 h. Crushed ice was added to quench the reaction, followed by a saturated aqueous solution of NH_4Cl (10 mL) and Et_2O (15 mL). The phases were separated, and the aqueous layer was extracted with Et_2O (2 × 20 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a yellow liquid, which was purified by column chromatography (PE/EtOAc = 9:1) to furnish pure aldehyde **15e** (277 mg, 68%) as a white solid. These data are in full accordance with those reported in the literature.[27] R_f = 0.38 (PE/EtOAc = 7:1); mp 147−149 °C (lit 146 °C); IR (neat) 2871, 1685, 1567, 1488, 1454, 1368, 1331, 1164, 1131, 1042 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.57 (s, 1H), 8.76 (s, 1H), 8.08 (dd, J = 8.8 and 1.2 Hz, 1H), 7.99 (dd, J = 8.4 and 1.2 Hz, 1H), 7.89 (ddd, J = 8.4, 6.8, and 1.6 Hz, 1H), 7.66 (ddd, J = 8.4, 7.2, and 1.2 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 189.3, 150.3, 149.7, 140.5, 133.8, 129.9, 128.8, 128.3, 126.7, 126.5; LRMS (EI) m/z (rel intensity) 193 ($[M]^{\cdot+}$, 32), 192 ($[M - H]^+$, 22), 191 ($[M]^{\cdot+}$, 84), 190 ($[M - H]^+$, 48), 162 ($[M - CHO]^+$, 38), 155 (40), 128 (32), 127 ($[M - Cl\text{-}CHO]^{\cdot+}$, 100), 101 (45), 100 (22), 76 (22), 75 (50), 74 (25), 51 (40), 50 (39).

*2-Chloro-1-phenyl-1H-imidazole (**S1**).* To a stirred solution of 1-phenyl-1*H*-imidazole (500 mg, 3.47 mmol, 1.0 equiv) in dry THF (30 mL) at −78 °C was added dropwise a solution of *n*-BuLi (2.5 M in hexanes, 1.53 mL, 3.82 mmol, 1.1 equiv), and the mixture was stirred at −78 °C for 20 min. A solution of hexachloroethane (2.46 g, 10.40 mmol, 3.0 equiv) in dry THF (10 mL) was slowly added, and the resulting mixture was stirred at −78 °C for 1 h then at rt for another 1 h. The reaction was quenched with ice, and a saturated aqueous solution of NH_4Cl (30 mL) was then added to the reaction mixture. The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 30 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give an orange solid, which was purified by column chromatography (PE/EtOAc = 1:1) to furnish pure chloroimidazole

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S1 (460 mg, 74%) as off-white crystals. These data are in full accordance with those reported in the literature.[18] R_f = 0.61 (PE/EtOAc = 1:1); mp 53−55 °C; IR (neat) 1594, 1495, 1454, 1374, 1307, 1285, 1117, 1088 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.51−7.42 (m, 3H), 7.36−7.34 (m, 2H), 7.09 (d, J = 1.6 Hz, 1H), 7.05 (d, J = 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 136.4, 131.8, 129.5 (2C), 128.9, 128.7, 125.8 (2C), 122.5; LRMS (EI) m/z (rel intensity) 180 ($[M]^{+\cdot}$, 34), 178 ($[M]^{+\cdot}$, 100), 153 (20), 151 (66), 124 (26), 116 (60), 90 (35), 89 (40), 77 (89), 75 (24), 63 (17), 51 (88), 50 (23).

*2-Chloro-1-phenyl-1H-imidazole-5-carbaldehyde (**15f**).* To a stirred solution of chloroimidazole **S1** (210 mg, 1.18 mmol, 1.0 equiv) in dry THF (12 mL) at −78 °C was added dropwise a solution of *n*-BuLi (2.5 M in hexanes, 0.49 mL, 1.23 mmol, 1.05 equiv), and the mixture was stirred at −78 °C for 40 min. Methylformate (0.15 mL, 2.35 mmol, 2 equiv) was slowly added, and the solution was stirred at −78 °C for 1 h then at rt for another 1 h. The reaction was quenched with ice, and a saturated aqueous solution of NH_4Cl (15 mL) was added to the reaction mixture. The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give an orange solid, which was purified by column chromatography (PE/EtOAc = 3:1) to furnish pure aldehyde **15f** (193 mg, 79%) as white crystals. R_f = 0.41 (PE/EtOAc = 2:1); mp 109−111 °C; IR (neat) 2866, 1670, 1599, 1526, 1494, 1430, 1394, 1375, 1361, 1281, 1150 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.53 (s, 1H), 7.80 (s, 1H), 7.55−7.50 (m, 3H), 7.31−7.27 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 177.4, 140.4, 140.0, 134.2, 133.8, 130.1, 129.5 (2C), 127.3 (2C); LRMS (EI) m/z (rel intensity) 208 ($[M]^{+\cdot}$, 11), 206 ($[M]^{+\cdot}$, 34), 205 (16), 171 ($[M - Cl]^+$, 2), 128 ($[M - Ph]^+$, 4), 116 (19), 89 (17), 78 (100), 77 (34), 51 (37); HRMS (ESI) calcd for $C_{10}H_8ClN_2O$ $[M + H]^+$ 207.0320, found 207.0320.

*3-Chloro-1-methyl-1H-pyrazole-4-carbaldehyde (**15g**).* To dry stirred DMF (0.47 mL, 6.12 mmol, 3.0 equiv) at −15 °C was added dropwise $POCl_3$ (1.33 mL, 14.27 mmol, 7.0 equiv). 3-Hydroxy-1-methyl-1*H*-pyrazole (200 mg, 2.04 mmol, 1.0 equiv) was then added, and the solution was refluxed for 2.5 h. After cooling to rt, the reaction was quenched with H_2O/ice, and the mixture was basified with aqueous NaOH 10 M (pH 10). The phases were separated, and the aqueous layer was further extracted with CH_2Cl_2 (2 × 30 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a dark brown oily residue, which was purified by column chromatography (PE/EtOAc = 1:1) to yield aldehyde **15g** as a white solid (227 mg, 77%). These data are in full accordance with those reported in the literature.[18] R_f = 0.43 (PE/EtOAc = 1:1); mp 99−101 °C; IR (neat) 2818, 1669, 1533, 1416, 1357, 1296, 1177, 1109 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.78 (s, 1H), 7.87 (s, 1H), 3.90 (d, J = 0.4 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 183.1, 141.8, 134.1, 119.7, 40.2; LRMS (EI) m/z (rel intensity) 146 ($[M]^{+\cdot}$, 18), 145 ($[M - H]^+$, 34), 144 ($[M]^{+\cdot}$, 60), 143 ($[M - H]^+$, 100), 51 (20).

*1-Acetyl-1H-indole-3-carbaldehyde (**15h**).* To an ice-cold stirred solution of 1*H*-indole-3-carbaldehyde (630 mg, 4.34 mmol, 1.0 equiv), DMAP (53 mg, 0.43 mmol, 0.1 equiv), and Et_3N (1.51 mL, 10.9 mmol, 2.5 equiv) in dry CH_2Cl_2 (30 mL) was slowly added Ac_2O (0.61 mL, 6.51 mmol, 1.5 equiv), and the resulting mixture was stirred at rt for 3 h. After complete conversion, the reaction was concentrated under reduced pressure to give a beige solid, which was purified by column chromatography (PE/EtOAc = 1:2) to yield acetamide **15h** as a white solid (709 mg, 87%). These data are in full accordance with those reported in the literature.[28] R_f = 0.71 (PE/EtOAc = 1:3); mp 165−167 °C (lit 167−169 °C); IR (neat) 2841, 1732, 1672, 1606, 1548, 1479, 1446, 1405, 1382, 1370, 1341, 1321, 1254, 1206, 1171, 1126, 1088, 1011 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.11 (s, 1H), 8.39 (dt_{app}, J = 7.6 and 0.8 Hz, 1H), 8.26 (ddd, J = 8.0, 1.6, and 0.8 Hz, 1H), 8.05 (s, 1H), 7.44 (td_{app}, J = 8.0 and 1.6 Hz, 1H), 7.40 (td_{app}, J = 7.6 and 1.6 Hz, 1H), 2.73 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 185.7, 168.7, 136.5, 135.3, 127.0, 126.1, 125.5, 122.8, 122.0, 116.5, 24.0; LRMS (EI) m/z (rel intensity) 187 ($[M]^{+\cdot}$, 39), 145 (77), 144 ($[M - CH_3CO]^+$, 100), 116 (24), 89 (31), 63 (16).

*1-Tosyl-1H-pyrrole-2-carbaldehyde (**15i**).* To an ice-cold stirred solution of 1*H*-pyrrole-2-carbaldehyde (500 mg, 5.26 mmol, 1.0 equiv) in dry THF (35 mL) was slowly added NaH (60% in mineral oil, 252 mg, 6.31 mmol, 1.2 equiv), and the mixture was stirred at 0 °C for 30 min. TsCl (1.20 g, 6.31 mmol, 1.2 equiv) was then added, and the solution was stirred at rt overnight. Crushed ice was added to quench the reaction, followed by the addition of a saturated aqueous solution of NH_4Cl (25 mL) and water (15 mL). The phases were separated, and the aqueous layer was extracted with Et_2O (2 × 35 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a beige solid, which was purified by column chromatography (PE/EtOAc = 4:1) to furnish *N*-tosylpyrrole **15i** (1.16 g, 89%) as white crystals. These data are in full accordance with those reported in the literature.[29] R_f = 0.34 (PE/EtOAc = 4:1); mp 91−93 °C (lit 92−94 °C); IR (neat) 1669, 1595, 1538, 1422, 1371, 1248, 1172, 1156, 1140, 1089, 1054, 1012 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.95 (s, 1H), 7.78 (dt_{app}, J = 8.4 and 2.0 Hz, 2H), 7.61 (dd, J = 3.2 and 2.0 Hz, 1H), 7.30 (bd, J = 8.0 Hz, 2H), 7.14 (dd, J = 3.6 and 2.0 Hz, 1H), 6.39 (t_{app}, J = 3.6 Hz, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 179.0, 146.0, 135.2, 133.5, 130.2 (2C), 129.5, 127.5 (2C), 124.6, 112.5, 21.7; LRMS (EI) m/z (rel intensity) 249 ($[M]^{+\cdot}$, 2), 155 ($[p\text{TolSO}_2]^+$, 16), 94 ($[M - p\text{TolSO}_2]^+$, 23), 92 (14), 91 ($[p\text{Tol}]^+$, 100), 65 ($[\text{pyrrole} - H]^{+\cdot}$, 31).

*1,3-Diphenylhex-5-en-1-one (**S2**).* To an ice-cold stirred solution of chalcone (1.00 g, 4.80 mmol, 1.0 equiv) and iodine (244 mg, 0.96 mmol, 0.2 equiv) in CH_2Cl_2 (35 mL) was added dropwise allyltrimethylsilane (1.07 mL, 6.72 mmol, 1.4 equiv), and the solution was stirred at rt for 4 h. A saturated aqueous solution of NH_4Cl (15 mL) and then an aqueous solution of $Na_2S_2O_3$ (10 mL) were added, and the mixture was stirred for 10 min. The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a pink residue, which was purified by column chromatography (PE/EtOAc = 20:1) to furnish pure ketone **S2** (880 mg, 73%) as a colorless oil. These data are in full accordance with those reported in the literature.[30] R_f = 0.53 (PE/EtOAc = 17:1); IR (neat) 1683, 1639, 1597, 1580, 1494, 1448, 1264, 1201, 1180, 1075, 999, 914 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.91−7.87 (m, 2H), 7.52 (tt_{app}, J = 8.4 and 1.2 Hz, 1H), 7.44−7.39 (m, 2H), 7.29−7.22 (m, 4H), 7.17 (m, 1H), 5.68 (ddt, J = 17.1, 10.2, and 7.0 Hz, 1H), 5.00 (ddt, J = 16.8, 2.0, and 1.6 Hz, 1H), 4.95 (ddt, J = 10.0, 2.0, and 1.1 Hz, 1H), 3.47 (quint, J = 7.1 Hz, 1H), 3.29 (dd, J = 7.0 and 1.4 Hz, 2H), 2.52−2.40 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 199.0, 144.5, 137.3, 136.4, 133.1, 128.6 (2C), 128.5 (2C), 128.1 (2C), 127.7 (2C), 126.5, 116.9, 44.7, 40.9, 40.8; LRMS (EI) m/z (rel intensity) 250 ($[M]^{+\cdot}$, 3), 130 (49), 105 ($[PhCO]^+$, 100), 77 ($[C_6H_5]^+$, 47), 51 (12).

*1,3-Diphenylhex-5-en-1-ol (**5**).* To an ice-cold stirred solution of ketone **S2** (900 mg, 3.60 mmol, 1.0 equiv) in EtOH (30 mL) was added $NaBH_4$ (163 mg, 4.31 mmol, 1.2 equiv), and the mixture was stirred at 50 °C for 1 h. The solution was evaporated under reduced pressure, and the residue was taken up in EtOAc (15 mL) and water (15 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 15 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give crude alcohol **5** as a colorless oil. The diastereomers were separated by column chromatography (PE/EtOAc = 8:1) to furnish pure alcohols *anti*-**5** (308 mg, 34%) and *syn*-**5** (471 mg, 52%) as colorless oils.

*anti-Diastereomer (anti-**5**).* These data are in full accordance with those reported in the literature.[31] R_f = 0.37 (PE/EtOAc = 8:1); IR (neat) 3377, 1639, 1602, 1493, 1453, 1050, 992 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.33−7.19 (m, 10H), 5.66 (ddt, J = 17.1, 10.2, and 7.0 Hz, 1H), 4.95 (m, 1H), 4.91 (m, 1H), 4.33 (bd_{app}, J = 10.2 Hz, 1H), 3.03 (dtd_{app}, J = 11.2, 7.3, and 4.1 Hz, 1H), 2.42−2.30 (m, 2H), 2.09 (ddd, J = 14.2, 10.3, and 4.1 Hz, 1H), 1.89−1.82 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 145.4, 144.5, 136.8, 128.6 (2C), 128.5 (2C), 128.0 (2C), 127.5, 126.4, 125.6 (2C), 116.3, 71.8, 45.5, 42.4, 41.8; LRMS (EI) m/z (rel intensity) 234 ($[M - H_2O]^{+\cdot}$, 2), 130

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(13), 107 ([PhCHOH]$^+$, 100), 105 ([PhCO]$^+$, 35), 91 (13), 79 (42), 77 ([C_6H_5]$^+$, 20).

*syn-Diastereomer (syn-**5**).* These data are in full accordance with those reported in the literature.[28] R_f = 0.29 (PE/EtOAc = 8:1); IR (neat) 3343, 1639, 1602, 1493, 1453, 1028, 996, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34−7.17 (m, 8H), 7.13−7.10 (m, 2H), 5.54 (ddt, J = 17.2, 10.1, and 7.0 Hz, 1H), 4.90 (m, 1H), 4.88 (m, 1H), 4.46 (bt_{app}, J = 7.2 Hz, 1H), 2.50 (m, 1H), 2.38−2.25 (m, 2H), 2.19−2.05 (m, 2H), 1.80 (bs, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 144.6, 144.3, 136.5, 128.61 (2C), 128.60 (2C), 127.90, 127.87 (2C), 126.48 (2C), 126.46, 116.4, 73.1, 44.7, 42.4, 41.7; LRMS (EI) m/z (rel intensity) 234 ([M − H_2O]$^{\cdot+}$, 2), 130 (12), 107 ([PhCHOH]$^+$, 100), 105 ([PhCO]$^+$, 37), 91 (16), 79 (45), 77 ([C_6H_5]$^+$, 24).

*4-Phenylbutane-1,2,4-triol (**S3**).* To a stirred solution of 1-phenyl-3-buten-1-ol (2.00 g, 13.50 mmol, 1.0 equiv) and NMO (1.90 g, 16.19 mmol, 1.2 equiv) in H_2O (5.5 mL) and acetone (22 mL) was slowly added a solution of OsO_4 (4% in H_2O, 843 μL, 0.14 mmol, 0.01 equiv), and the mixture was stirred at rt overnight. The reaction was quenched with an aqueous solution of $Na_2S_2O_3$ (25 mL), and EtOAc (60 mL) was added. The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 40 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a brown residue, which was purified by column chromatography (PE/EtOAc = 1:4 to pure EtOAc) to furnish desired triol **S3** (2.02 g, 82%) as a waxy residue as a 50:50 mixture of diastereomers.These data are in full accordance with those reported in the literature.[32] R_f = 0.33 and 0.26 (EtOAc); IR (neat) 3321, 1604, 1494, 1453, 1331, 1205, 1101, 1054, 1025, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.26−7.16 (m, 5H), 4.90 (bs, 0.5H), 4.79 (m, 1H), 4.71 (m, 1H), 4.62 (bd, J = 3.6 Hz, 0.5H), 4.42 (bs, 0.5H), 4.27 (bs, 0.5H), 3.94 (bs, 0.5H), 3.80 (bs, 0.5H), 3.48−3.32 (m, 2H), 1.81 (dt_{app}, J = 14.4 and 9.4 Hz, 0.5H), 1.71−1.58 (m, 1.5H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ [144.6 and 144.1], [128.6 (2C) and 128.5 (2C)], [127.7 and 127.4], [125.9 (2C) and 125.7 (2C)], [73.6 and 70.5], [72.0 and 69.3], [66.8 and 66.5], [41.7 and 41.4]; LRMS (EI) m/z (rel intensity) 164 ([M − H_2O]$^{\cdot+}$, 23), 163 (28), 120 (20), 117 (15), 115 (24), 107 ([PhCHOH]$^+$, 20), 105 ([PhCO]$^+$, 77), 104 ([PhC_2H_3]$^{\cdot+}$, 100), 103 (51), 92 (55), 91 (51), 89 (17), 79 (51), 78 (95), 77 ([C_6H_5]$^+$, 81), 63 (25), 57 (16), 52 (24), 51 (88), 50 (38).

*1-Phenylhex-5-ene-1,3-diol (**10**).* To a stirred solution of triol **S3** (1.99 g, 10.92 mmol, 1.0 equiv) in THF/H_2O (1:1, 80 mL) was added $NaIO_4$ (9.34 g, 43.68 mmol, 4.0 equiv). The mixture was stirred at rt for 1 h before adding EtOAc (30 mL) and H_2O (30 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 50 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a yellow oil. The crude aldehyde was diluted in dry THF (50 mL), and the solution was cooled to −78 °C. Allylmagnesium chloride (2 M in THF, 16.0 mL, 31.96 mmol, 3.2 equiv) was added dropwise, and the solution was stirred at −78 °C for 1 h and then at rt for 30 min. The reaction was quenched with ice, and a saturated aqueous solution of NH_4Cl (40 mL) was added to the reaction mixture. The phases were separated, and the aqueous layer was extracted with Et_2O (2 × 40 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give an orange oil, which was purified by column chromatography (PE/EtOAc = 3:1) to furnish diol **10** (1.30 g, 64%) as a colorless oil as a 50:50 mixture of diastereomers. These data are in full accordance with those reported in the literature.[33] R_f = 0.29 and 0.24 (PE/EtOAc = 2:1); IR (neat) 3334, 1643, 1605, 1496, 1454, 1326, 1205, 1060, 996, 915 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35−7.34 (m, 4H), 7.27 (m, 1H), 5.78 (m, 1H), 5.15−5.08 (m, 2H), 5.03 ($quint_{app}$, J = 3.8 Hz, 0.5H), 4.91 (ddd, J = 8.8, 4.4, and 1.8 Hz, 0.5H), 3.93 (m, 1H), 3.73 (d, J = 2.0 Hz, 0.5H), 3.37 (d, J = 4.3 Hz, 0.5H), 3.31 (d, J = 2.6 Hz, 0.5H), 2.69 (d, J = 4.0 Hz, 0.5H), 2.28−2.22 (m, 2H), 1.94−1.75 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ [144.6 and 144.5], [134.5 and 134.2], [128.6 (2C) and 128.5 (2C)], [127.7 and 127.4], [125.8 (2C) and 125.6 (2C)], [118.5 and 118.4], [75.2 and 71.7], [71.6 and 68.1], [44.9 and 44.1], [42.5 and 42.0]; LRMS (EI) m/z (rel intensity) 174 ([M − H_2O]$^{\cdot+}$, 3), 149 (38), 133 (24), 120 (10), 107 ([PhCHOH]$^+$, 100), 106 (13), 105 ([PhCO]$^+$, 99), 104 ([PhC_2H_3]$^{\cdot+}$, 12), 79 (80), 78 (13), 77 ([C_6H_5]$^+$, 47), 68 (19), 67 (20), 51 (13).

*4-Allyl-2,2-dimethyl-6-phenyl-1,3-dioxane (**9**).* To a stirred solution of diol **10** (1.25 g, 6.50 mmol, 1.0 equiv) and 2,2-dimethoxypropane (8.06 mL, 65.02 mmol, 10.0 equiv) in CH_2Cl_2 (35 mL) was added PPTS (163 mg, 0.65 mmol, 0.1 equiv), and the solution was stirred at rt for 20 h. A saturated aqueous solution of NH_4Cl (15 mL) and H_2O (10 mL) were added; the phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a pale yellow oil, which was purified by column chromatography (PE/EtOAc = 14:1) to furnish acetonide **9** (1.31 g, 87%) as a colorless oil as a 50:50 mixture of diastereomers. R_f = 0.50 (PE/EtOAc = 14:1); IR (neat) 1643, 1606, 1496, 1451, 1378, 1252, 1225, 1200, 1168, 1100, 1071, 1019, 960, 913 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.32 (m, 4H), 7.26 (m, 1H), 5.83 (m, 1H), 5.15−5.04 (m, 2H), 4.88 (m, 1H), 4.04 (m, 1H), 2.38 (m, 1H), 2.23 (m, 1H), 1.96 (m, 1H), 1.75 (dt_{app}, J = 13.2 and 2.5 Hz, 0.5H), 1.56 (s, 1.5H), 1.52 (s, 1.5H), 1.46 (s, 1.5H), 1.45 (s, 1.5H), 1.45 (dt, J = 13.3 and 11.5 Hz, 0.5H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ [142.7 and 142.5], [134.4 and 134.1], 128.5 (2C), [127.7 and 127.5], [126.1 (2C) and 126.0 (2C)], [117.4 and 117.2], [100.9 and 99.1], [71.7 and 68.7], [68.9 and 66.5], [40.9 and 40.3], [39.6 and 39.0], [30.4 and 25.3], [24.9 and 19.9]; LRMS (EI) m/z (rel intensity) 217 ([M − CH_3]$^+$, 7), 174 ([M − acetone]$^{\cdot+}$, 17), 157 ([M − acetone − OH]$^+$, 27), 133 (32), 129 (33), 115 (41), 107 (68), 105 ([PhCO]$^+$, 100), 104 ([PhC_2H_3]$^{\cdot+}$, 37), 103 (18), 91 (44), 79 (25), 78 (20), 77 ([C_6H_5]$^+$, 34), 68 (93), 67 (50), 59 (62); HRMS (ESI) calcd for $C_{15}H_{20}O_2Na$ [M + Na]$^+$ 255.1356, found 255.1356

*4-Allyl-2,2-dimethyl-6-phenyl-1,3-dioxane (*cis*-**9**).* To an ice-cold stirred solution of acetonide **9** (600 mg, 2.58 mmol, 1.0 equiv) in CH_2Cl_2 (200 mL) was added a 2 M aqueous solution of HCl (65 μL, 0.13 mmol, 0.05 equiv), and the solution was vigorously stirred at 0 °C for 3 h. A saturated aqueous solution of Na_2CO_3 (15 mL) and H_2O (85 mL) were added; the phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a yellow oil, which was purified by column chromatography (PE/EtOAc = 14:1 then 2:1) to furnish pure acetonide *cis*-**9** (214 mg, 36%) and diol *anti*-**10** (145 mg, 29%) as colorless oils. R_f = 0.50 (PE/EtOAc = 14:1); IR (neat) 1643, 1605, 1496, 1452, 1378, 1252, 1198, 1167, 1101, 1071, 1046, 961, 913 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42−7.35 (m, 4H), 7.29 (tt_{app}, J = 6.8 and 2.0 Hz, 1H), 5.86 (dddd, J = 17.2, 10.3, 7.6, and 6.6 Hz, 1H), 5.12 (m, 1H), 5.09 (m, 1H), 4.92 (dd, J = 11.7 and 2.8 Hz, 1H), 4.07 (dtd, J = 11.5, 6.3, and 2.4 Hz, 1H), 2.40 (dtt_{app}, J = 14.0, 6.3, and 1.5 Hz, 1H), 2.22 (dddt, J = 14.1, 7.6, 6.7, and 1.4 Hz, 1H), 1.78 (dt_{app}, J = 13.2 and 2.5 Hz, 1H), 1.59 (s, 3H), 1.55 (s, 3H), 1.48 (dt_{app}, J = 13.1 and 11.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 142.5, 134.1, 128.5 (2C), 127.7, 126.0 (2C), 117.4, 99.1, 71.6, 68.9, 40.9, 39.0, 30.4, 19.9; LRMS (EI) m/z (rel intensity) 217 ([M − CH_3]$^+$, 10), 174 ([M − acetone]$^{\cdot+}$, 1), 157 ([M − acetone − OH]$^+$, 17), 133 (17), 129 (19), 115 (29), 105 ([PhCO]$^+$, 72), 104 ([PhC_2H_3]$^{\cdot+}$, 100), 103 (50), 91 (37), 79 (23), 78 (78), 77 ([C_6H_5]$^+$, 62), 68 (29), 67 (24), 63 (17), 59 (30), 58 (38), 52 (22), 51 (71), 50 (33); HRMS (ESI) calcd for $C_{15}H_{20}O_2Na$ [M + Na]$^+$ 255.1356, found 255.1357

*1-Phenylhex-5-ene-1,3-diol (*anti*-**10**).* These data are in full accordance with those reported in the literature.[34] R_f = 0.24 (PE/EtOAc = 2:1); IR (neat) 3346, 1641, 1603, 1494, 1452, 1323, 1207, 1050, 994 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (d_{app}, J = 4.3 Hz, 4H), 7.26 (m, 1H), 5.77 (ddt, J = 16.0, 11.6, and 6.8 Hz, 1H), 5.13−5.07 (m, 2H), 5.01 (bd_{app}, J = 8.0 Hz, 1H), 3.90 (bq_{app}, J = 7.1 Hz, 1H), 3.72 (bd_{app}, J = 2.8 Hz, 1H), 3.01 (bs, 1H), 2.26−2.22 (m, 2H), 1.92−1.78 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 144.6, 134.5, 128.5 (2C), 127.3, 125.6 (2C), 118.2, 71.4, 68.0, 44.2, 42.0; LRMS (EI) m/z (rel intensity) 174 ([M − H_2O]$^{\cdot+}$, 2), 156 ([M − $2H_2O$]$^{\cdot+}$, 19), 115 ([M − Ph]$^+$, 19), 107 ([PhCHOH]$^+$, 32), 106 (28),

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105 ([PhCO]$^+$, 100), 104 ([PhC_2H_3]$^{\cdot+}$, 62), 103 (42), 91 (30), 79 (46), 78 (59), 77 ([C_6H_5]$^+$, 89), 76 (15), 63 (19), 52 (22), 51 (86), 50 (41).

*1-Phenylhex-5-ene-1,3-diol (syn-**10**).* To an ice-cold stirred solution of acetonide *cis*-**9** (200 mg, 0.86 mmol, 1.0 equiv) in THF (15 mL) was added a 1 M aqueous solution of HCl (4.3 mL, 4.30 mmol, 5.0 equiv), and the solution was stirred at rt. After 18 h, a saturated aqueous solution of Na_2CO_3 (5 mL) and H_2O (5 mL) were added; the phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a yellow oil, which was purified by column chromatography (PE/EtOAc = 2:1) to furnish diol *syn*-**10** (137 mg, 83%) as a colorless oil. These data are in full accordance with those reported in the literature.[31] R_f = 0.29 (PE/EtOAc = 2:1); IR (neat) 3262, 1640, 1494, 1446, 1366, 1332, 1287, 1202, 1114, 1097, 1065, 1033, 1003, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (d_{app}, J = 4.4 Hz, 4H), 7.26 (m, 1H), 5.76 (ddt, J = 17.6, 9.6, and 7.2 Hz, 1H), 5.11−5.05 (m, 2H), 4.85 (ddd, J = 9.4, 4.0, and 2.0 Hz, 1H), 4.08 (d, J = 2.1 Hz, 1H), 3.91 (m, 1H), 3.64 (d, J = 2.7 Hz, 1H), 2.21 (ddt_{app}, J = 7.2, 6.0, and 1.2 Hz, 2H), 1.83−1.73 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 144.5, 134.2, 128.5 (2C), 127.6, 125.8 (2C), 118.2, 75.0, 71.6, 44.7, 42.4; LRMS (EI) m/z (rel intensity) 156 ([M − $2H_2O$]$^{\cdot+}$, 15), 133 (18), 115 ([M − Ph]$^+$,13), 107 ([PhCHOH]$^+$, 39), 106 (25), 105 ([PhCO]$^+$, 100), 104 ([PhC_2H_3]$^{\cdot+}$, 43), 103 (30), 91 (25), 79 (61), 78 (44), 77 ([C_6H_5]$^+$, 87), 68 (15), 52 (16), 51 (58), 50 (27).

*Grignard Reagent **S4**.* The Grignard reagent **S4** was synthesized by reacting 5-bromopentene (1.0 equiv) with magnesium turnings (2.0 equiv) and one crystal of iodine in refluxing dry Et_2O (0.5 M) for 1.5 h. The mixture was then cooled to rt and decanted to furnish a clear gray solution of 4-pentenylmagnesium bromide **S4** in Et_2O, which was used immediately.

General Procedure 1 (GP1). *Synthesis of Alcohols **16b**−**16j**.* To a stirred solution of aldehyde (1.0 equiv) in dry Et_2O (0.3 M) at −78 °C was added dropwise a solution of 4-pentenylmagnesium bromide **S4** (1.5 to 2.0 equiv) in Et_2O. The mixture was stirred at −78 °C for 30 min and then at rt for 1.5 h. The reaction was quenched with ice, and a saturated aqueous solution of NH_4Cl (20 mL) was added to the reaction mixture. The phases were separated, and the aqueous layer was further extracted with EtOAc (2 × 30 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give an orange oily residue, which was purified by column chromatography to yield the desired alcohol.

*1-(2-Chloropyridin-3-yl)hex-5-en-1-ol (**16b**).* This compound was prepared according to GP1 using 2-chloro-3-pyridinecarboxaldehyde **15b** (400 mg, 2.83 mmol). The crude product was purified by column chromatography (CH_2Cl_2/EtOAc = 5:1) to furnish pure alcohol **16b** (535 mg, 89%) as a colorless oil. R_f = 0.48 (CH_2Cl_2/EtOAc = 5:1); IR (neat) 3334, 1640, 1567, 1407, 1337, 1260, 1185, 1116, 1058, 993 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.17 (dd, J = 4.8 and 2.0 Hz, 1H), 7.91 (ddd, J = 7.6, 2.0, and 0.4 Hz, 1H), 7.22 (ddd, J = 7.6, 4.8, and 0.4 Hz, 1H), 5.76 (ddt, J = 17.2, 10.0, and 6.4 Hz, 1H), 5.03 (dt_{app}, J = 7.6 and 4.0 Hz, 1H), 4.97 (dq_{app}, J = 16.8 and 1.6 Hz, 1H), 4.92 (ddt, J = 10.0, 2.0, and 1.2 Hz, 1H), 3.38 (d, J = 4.0 Hz, 1H), 2.14−2.00 (m, 2H), 1.76 (m, 1H), 1.68−1.43 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 148.6, 148.0, 139.5, 138.4, 136.5, 123.0, 114.9, 69.7, 36.9, 33.4, 24.9; LRMS (EI) m/z (rel intensity) 211 ([M]$^{\cdot+}$, 1), 168 (21), 155 (17), 144 ([M − C_5H_9]$^+$, 32), 142 ([M − C_5H_9]$^+$, 100), 139 (15), 106 (63), 78 (51), 51 (24); HRMS (ESI) calcd for $C_{11}H_{15}ClNO$ [M + H]$^+$ 212.0837, found 212.0837.

*1-(4,6-Dichloropyrimidin-5-yl)hex-5-en-1-ol (**16c**).* This compound was prepared according to GP1 using 4,6-dichloropyrimidine-5-carboxaldehyde **15c** (400 mg, 2.26 mmol). The crude product was purified by column chromatography (PE/EtOAc = 6:1) to furnish pure alcohol **16c** (162 mg, 29%) as a colorless oil. R_f = 0.36 (PE/EtOAc = 6:1); IR (neat) 3407, 1640, 1514, 1415, 1331, 1225, 1132, 1071, 993 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.65 (s, 1H), 5.76 (ddt, J = 16.8, 10.0, and 6.8 Hz, 1H), 5.30 (bt, J = 6.8 Hz, 1H), 5.00 (dq_{app}, J = 17.2 and 2.0 Hz, 1H), 4.96 (ddt, J = 10.4, 2.4, and 1.6 Hz, 1H), 2.82 (bs, 1H, OH), 2.14−2.03 (m, 3H), 1.86 (ddt, J = 13.6, 10.4, and 6.0 Hz, 1H), 1.66 (m, 1H), 1.40 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 160.7 (2C), 156.4, 137.9, 133.4, 115.4, 70.3, 34.2, 33.2, 25.1; LRMS (EI) m/z (rel intensity) 228 ([M − H_2O]$^{\cdot+}$, 1), 213 ([M − Cl]$^+$, 4), 211 ([M − Cl]$^+$, 4), 181 ([M − C_5H_9]$^+$, 5), 179 ([M − C_5H_9]$^+$, 30), 177 ([M − C_5H_9]$^+$, 48), 141 (18), 86 (27), 67 (17), 55 (17), 54 (100); HRMS (ESI) calcd for $C_{10}H_{13}Cl_2N_2O$ [M + H]$^+$ 247.0399, found 247.0400

*1-(1-Chloroisoquinolin-7-yl)hex-5-en-1-ol (**16d**).* This compound was prepared according to GP1 using aldehyde **15d** (350 mg, 1.83 mmol). The crude product was purified by column chromatography (PE/EtOAc = 6:1) to furnish pure alcohol **16d** (395 mg, 83%) as a colorless oil. R_f = 0.40 (PE/EtOAc = 4:1); IR (neat) 3337, 2858, 1589, 1551, 1438, 1413, 1305, 1258, 1227, 1161, 1066, 993 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.23−8.21 (m, 2H), 7.81 (bd, J = 8.4 Hz, 1H), 7.76 (dd, J = 8.8 and 2.0 Hz, 1H), 7.56 (dd, J = 5.6 and 0.8 Hz, 1H), 5.77 (ddt, J = 17.2, 10.0, and 6.4 Hz, 1H), 5.00 (dq_{app}, J = 17.2 and 1.6 Hz, 1H), 4.95 (ddt, J = 10.0, 2.0, and 1.2 Hz, 1H), 4.93 (bdd, J = 7.6 and 5.6 Hz, 1H), 2.43 (bs, 1H, OH), 2.10 (qt_{app}, J = 6.8 and 1.2 Hz, 2H), 1.93−1.76 (m, 2H), 1.58 (m, 1H), 1.43 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 151.6, 145.7, 141.4, 138.4, 137.4, 129.7, 127.5, 126.9, 123.0, 120.7, 115.1, 74.3, 38.7, 33.6, 25.1; LRMS (EI) m/z (rel intensity) 263 ([M]$^{\cdot+}$, 2), 261 ([M]$^{\cdot+}$, 7), 245 ([M − H_2O]$^{\cdot+}$, 9), 243 ([M − H_2O]$^{\cdot+}$, 25), 218 (35), 207 (14), 205 (46), 204 (16), 202 (45), 194 ([M − C_5H_9]$^+$, 27), 192 ([M − C_5H_9]$^+$, 91), 191 ([1-chloroisoquinolineC_2H_3]$^{\cdot+}$, 17), 190 (22), 189 ([1-chloroisoquinolineC_2H_3]$^{\cdot+}$, 34), 166 (41), 164 (25), 129 ([isoquinoline]$^{\cdot+}$, 13), 128 ([isoquinoline − H]$^+$, 100), 101 (20), 77 ([C_6H_5]$^+$, 18); HRMS (ESI) calcd for $C_{15}H_{17}ClNO$ [M + H]$^+$ 262.0993, found 262.0997

*1-(2-Chloroquinolin-3-yl)hex-5-en-1-ol (**16e**).* This compound was prepared according to GP1 using aldehyde **15e** (230 mg, 1.20 mmol). The crude product was purified by column chromatography (pentane/EtOAc = 6:1) to furnish pure alcohol **16e** (143 mg, 46%) as a colorless oil. R_f = 0.43 (PE/EtOAc = 6:1); IR (neat) 3343, 3065, 1639, 1619, 1589, 1563, 1491, 1397, 1325, 1205, 1137, 1070, 1037 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.28 (s, 1H), 7.90 (dd, J = 8.8 and 1.2 Hz, 1H), 7.69 (dd, J = 8.0 and 1.6 Hz, 1H), 7.63 (ddd, J = 8.4, 6.8, and 1.6 Hz, 1H), 7.47 (ddd, J = 8.0, 6.8, and 1.2 Hz, 1H), 5.76 (ddt, J = 17.2, 10.4, and 6.8 Hz, 1H), 5.15 (bdt, J = 8.0 and 3.2 Hz, 1H), 4.98 (dq_{app}, J = 17.2 and 1.6 Hz, 1H), 4.92 (ddt, J = 10.0, 2.0, and 1.2 Hz, 1H), 3.53 (d, J = 3.6 Hz, 1H, OH), 2.16−2.01 (m, 2H), 1.86 (m, 1H), 1.72−1.50 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 148.8, 146.6, 138.4, 137.0, 135.8, 130.2, 127.8, 127.7, 127.4, 127.1, 114.9, 70.0, 37.2, 33.4, 25.1; LRMS (EI) m/z (rel intensity) 261 ([M]$^{\cdot+}$, 7), 245 ([M − H_2O]$^{\cdot+}$, 15), 243 ([M − H_2O]$^{\cdot+}$, 45), 218 (18), 207 (17), 206 (18), 205 (28), 204 (25), 202 (62), 194 ([M − C_5H_9]$^+$, 29), 192 ([M − C_5H_9]$^+$, 100), 191 ([chloroquinolineC_2H_3]$^{\cdot+}$, 28), 190 (21), 189 ([chloroquinolineC_2H_3]$^{\cdot+}$, 68), 180 (16), 167 (41), 166 (31), 156 (70), 154 (20), 140 (22), 128 ([quinoline − H]$^+$, 81), 101 (38), 77 ([C_6H_5]$^+$, 25) 75 (20), 51 (20); HRMS (ESI) calcd for $C_{15}H_{17}ClNO$ [M + H]$^+$ 262.0993, found 262.0996

*1-(2-Chloro-1-phenyl-1H-imidazol-5-yl)hex-5-en-1-ol (**16f**).* This compound was prepared according to GP1 using aldehyde **15f** (310 mg, 1.50 mmol). The crude product was purified by column chromatography (PE/EtOAc = 3:1) to furnish pure alcohol **16f** (322 mg, 78%) as white crystals. R_f = 0.39 (PE/EtOAc = 3:1); mp 100−102 °C; IR (neat) 3179, 1597, 1563, 1498, 1454, 1395, 1279, 1073, 987 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52−4.49 (m, 3H), 7.31 (bs, 2H), 6.92 (d, J = 0.4 Hz, 1H), 5.70 (ddt, J = 17.2, 10.4, and 6.4 Hz, 1H), 4.93 (dq_{app}, J = 17.2 and 2.0 Hz, 1H), 4.90 (ddt, J = 10.0, 2.0, and 1.6 Hz, 1H), 4.33 (bt, J = 7.2 Hz, 1H), 3.08 (bs, 1H, OH), 1.98 (bq_{app}, J = 6.8 Hz, 2H), 1.79−1.66 (m, 2H), 1.47 (m, 1H), 1.35 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 138.3, 138.0, 134.9, 133.0, 129.7 (2C), 129.5 (2C), 128.2, 125.3, 115.0, 64.9, 35.2, 33.3, 25.1; LRMS (EI) m/z (rel intensity) 276 ([M]$^{\cdot+}$, 4), 260 ([M − H_2O]$^{\cdot+}$, 5), 258 ([M − H_2O]$^{\cdot+}$, 16), 241 ([M − Cl]$^+$, 3), 219 (31), 218 (14), 217 (96), 209 ([M − C_5H_9]$^+$, 19), 207 ([M − C_5H_9]$^+$, 60), 179 (25), 156 (31), 138 (30), 129 (17), 78 (20), 77 ([C_6H_5]$^+$, 100), 51 (43); HRMS (ESI) calcd for $C_{15}H_{18}ClN_2O$ [M + H]$^+$ 277.1102, found 277.1107

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*1-(3-Chloro-1-methyl-1H-pyrazol-4-yl)hex-5-en-1-ol (**16g**).* This compound was prepared according to GP1 using aldehyde **15g** (280 mg, 1.94 mmol). The crude product was purified by column chromatography (PE/EtOAc = 1:1) to furnish pure alcohol **16g** (394 mg, 95%) as a yellow oil. R_f = 0.23 (PE/EtOAc = 1:1); IR (neat) 3372, 3077, 1640, 1557, 1407, 1315, 1175, 1068, 1001, 910 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.27 (s, 1H), 5.76 (ddt, J = 16.8, 10.0, and 6.8 Hz, 1H), 4.98 (dq_{app}, J = 17.2 and 1.6 Hz, 1H), 4.92 (ddt, J = 10.0, 2.0, and 1.2 Hz, 1H), 4.63 (dd, J = 7.6 and 6.4 Hz, 1H), 3.78 (s, 3H), 2.55 (bs, 1H, OH), 2.06 (qt_{app}, J = 7.2 and 1.6 Hz, 2H), 1.82−1.66 (m, 2H), 1.50 (m, 1H), 1.38 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 138.5, 136.6, 129.6, 122.4, 114.8, 65.5, 39.6, 37.1, 33.5, 24.9; LRMS (EI) m/z (rel intensity) 198 ($[M - H_2O]^{\cdot+}$, 10), 196 ($[M - H_2O]^{\cdot+}$, 32), 157 (34), 155 (100), 147 ($[M - C_5H_9]^+$, 15), 145 ($[M - C_5H_9]^+$, 53), 144 (22), 143 (19), 142 (62), 129 (21), 128 (16), 120 (30), 119 (37), 116 (16), 114 (38), 92 (17), 78 (17), 77 (19), 65 (17), 51 (20); HRMS (ESI) calcd for $C_{10}H_{16}ClN_2O$ $[M + H]^+$ 215.0946, found 215.0945

*1-(3-(1-Hydroxyhex-5-en-1-yl)-1H-indol-1-yl)ethanone (**16h**).* This compound was prepared according to GP1 using aldehyde **15h** (300 mg, 1.60 mmol). The crude product was purified by column chromatography (PE/EtOAc = 3:1) to furnish pure alcohol **16h** (198 mg, 48%) as a yellow oil. R_f = 0.46 (PE/EtOAc = 2:1); IR (neat) 3400, 1689, 1605, 1450, 1384, 1329, 1241, 1218, 1126, 1007, 935 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.42 (d, J = 8.0 Hz, 1H), 7.64 (ddd, J = 7.6, 1.2, and 0.8 Hz, 1H), 7.36 (ddd, J = 8.4, 7.6, and 1.2 Hz, 1H), 7.30 (s, 1H), 7.28 (ddd, J = 8.0, 7.2, and 1.2 Hz, 1H), 5.80 (ddt, J = 17.2, 10.4, and 6.8 Hz, 1H), 5.01 (dq_{app}, J = 17.2 and 1.6 Hz, 1H), 4.98−4.95 (m, 2H), 2.55 (s, 3H), 2.15−2.09 (m, 3H), 1.97−1.90 (m, 2H), 1.62 (m, 1H), 1.51 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.8, 138.6, 136.4, 128.7, 126.3, 125.5, 123.7, 121.7, 119.8, 116.9, 115.0, 68.0, 36.9, 33.6, 25.2, 24.1; LRMS (EI) m/z (rel intensity) 257 ($[M]^{\cdot+}$, 4), 239 ($[M - H_2O]^{\cdot+}$, 21), 198 (24), 156 (100), 146 (27), 143 (16), 129 (49), 128 (22), 118 (21); HRMS (ESI) calcd for $C_{16}H_{19}NO_2Na$ $[M + Na]^+$ 280.1308, found 280.1308

*1-(1-Tosyl-1H-pyrrol-2-yl)hex-5-en-1-ol (**16i**).* This compound was prepared according to GP1 using aldehyde **15i** (380 mg, 1.52 mmol). The crude product was purified by column chromatography (PE/EtOAc = 4:1) to furnish pure alcohol **16i** (298 mg, 61%) as a colorless oil. R_f = 0.51 (PE/EtOAc = 4:1); IR (neat) 3414, 1640, 1597, 1364, 1173, 1150, 1089, 1055, 910 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.66 (dt_{app}, J = 8.4 and 2.0 Hz, 2H), 7.29−7.27 (m, 3H), 6.26 (ddd, J = 3.2, 1.6, and 0.4 Hz, 1H), 6.23 (td, J = 3.2 and 0.4 Hz, 1H), 5.73 (ddt, J = 16.8, 10.0, and 6.8 Hz, 1H), 4.94 (dq_{app}, J = 16.8 and 2.0 Hz, 1H), 4.91 (ddt, J = 10.0, 2.0, and 1.2 Hz, 1H), 4.82 (m, 1H), 2.85 (d, J = 4.0 Hz, 1H), 2.39 (s, 3H), 2.06−1.91 (m, 2H), 1.87−1.72 (m, 2H), 1.48 (m, 1H), 1.37 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 145.2, 138.5, 138.2, 136.3, 130.1 (2C), 126.6 (2C), 123.4, 114.7, 112.3, 111.6, 65.1, 34.6, 33.3, 25.3, 21.7; LRMS (EI) m/z (rel intensity) 301 ($[M - H_2O]^{\cdot+}$, 6), 260 (44), 155 ($[p\text{TolSO}_2]^+$, 30), 105 (16), 104 (17), 92 (15), 91 ($[p\text{Tol}]^+$, 100), 65 ($[\text{pyrrole} - H]^{\cdot+}$, 36); HRMS (ESI) calcd for $C_{17}H_{21}NO_3SNa$ $[M + Na]^+$ 342.1134, found 342.1133

*1-Phenylhex-5-en-1-ol (**16j**).* This compound was prepared according to GP1 using benzaldehyde (508 mg, 4.79 mmol). The crude product was purified by column chromatography (PE/EtOAc = 5:1) to furnish pure alcohol **16j** (673 mg, 80%) as a colorless oil. These data are in full accordance with those reported in the literature.[35] R_f = 0.35 (PE/EtOAc = 6:1); IR (neat) 3344, 2934, 2860, 1640, 1493, 1454, 1201, 1062, 1027, 993 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.26 (m, 5H), 5.79 (ddt, J = 17.2, 10.4, and 6.4 Hz, 1H), 5.00 (ddt, J = 17.2, 2.4, and 1.6 Hz, 1H), 4.95 (ddt, J = 10.0, 2.4, and 1.2 Hz, 1H), 4.66 (dd, J = 7.2 and 5.6 Hz, 1H), 2.08 (qt_{app}, J = 7.2 and 1.2 Hz, 2H), 2.04 (s, 1H, OH), 1.86−1.68 (m, 2H), 1.53 (m, 1H), 1.39 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 144.9, 138.7, 128.5 (2C), 127.6, 126.0 (2C), 114.8, 74.6, 38.6, 33.7, 25.2; LRMS (EI) m/z (rel intensity) 176 ($[M]^{\cdot+}$, 2), 158 ($[M - H_2O]^{\cdot+}$, 17), 133 (22), 120 (21), 117 ($[M - H_2O - C_3H_5]^+$, 53), 115 (28), 107 ($[M - C_5H_9]^+$, 100), 105 (19), 104 ($[PhC_2H_3]^{\cdot+}$, 38), 91 (21), 79 (71), 77 ($[C_6H_5]^+$, 40), 51 (16).

*1-(4-Chloro-7-(phenylsulfonyl)-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-allyl Acetate (**19**).* To an ice-cold stirred solution of 1-(4-chloro-7-(phenylsulfonyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)prop-2-en-1-ol (70 mg, 0.20 mmol, 1.0 equiv), DMAP (2.4 mg, 0.02 mmol, 0.1 equiv), and Et_3N (70 μL, 0.50 mmol, 2.5 equiv) in dry CH_2Cl_2 (1.5 mL) was slowly added Ac_2O (28 μL, 0.30 mmol, 1.5 equiv), and the resulting mixture was stirred at 0 °C for 1 h. After complete conversion, the reaction was concentrated under reduced pressure to give a yellow solid, which was purified by column chromatography on neutralized silica gel (PE/EtOAc = 2:1) to yield allylic acetate **19** as white crystals (78 mg, 99%). R_f = 0.38 (PE/EtOAc = 2:1); mp 155−157 °C; IR (neat) 1738, 1591, 1542, 1436, 1384, 1229, 1155, 1092, 1017, 935 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.75 (s, 1H), 8.22 (m, 2H), 7.78 (d, J = 0.8 Hz, 1H), 7.66 (tt, J = 7.6 and 2.0 Hz, 1H), 7.55 (m, 2H), 6.71 (dq_{app}, J = 5.6 and 1.2 Hz, 1H), 6.13 (ddd, J = 17.2, 10.4, and 6.0 Hz, 1H), 5.40 (dt_{app}, J = 10.8 and 1.2 Hz, 1H), 5.38 (ddd, J = 17.2, 1.2, and 0.8 Hz, 1H), 2.12 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 169.7, 152.9, 152.8, 151.7, 137.2, 135.2, 133.8, 129.5 (2C), 128.6 (2C), 126.0, 119.1, 117.6, 116.7, 68.3, 21.2; LRMS (EI) m/z (rel intensity) 333 ($[M - AcOH]^{\cdot+}$, 4), 331 ($[M - AcOH]^{\cdot+}$, 13), 208 (28), 191 (15), 190 (29), 141 ($[PhSO_2]^+$, 28), 78 (13), 77 ($[C_6H_5]^+$, 100), 51 (27); HRMS (ESI) calcd for $C_{17}H_{14}ClN_3O_4SNa$ $[M + Na]^+$ 414.0286, found 414.0286.

General Procedure 2 (GP2). *Synthesis of Hydroxy Allylic Acetates **3**, **6**, **11**, **17b−17j** by Cross-Metathesis.* To a stirred solution of alcohol (1.0 equiv) and 1-phenylallyl acetate **S5**[36] or allylic acetate **19** (3.0 equiv) in dry CH_2Cl_2 (0.7 M) in a sealed tube under argon was added Grubbs−Hoveyda II catalyst (10 mol %). The mixture was stirred at 50 °C for 24 h and cooled to rt, and the solvent was removed under reduced pressure to give a dark green oil, which was purified by column chromatography on neutralized silica gel to yield the desired hydroxy allylic acetate.

*(E)-7-Hydroxy-1,7-diphenylhept-2-en-1-yl Acetate (**3**).* This compound was prepared according to GP2 using alcohol **16j** (200 mg, 1.14 mmol) and allylic acetate **S5**. The product was purified by column chromatography (PE/EtOAc = 5:1) to furnish pure olefin **3** (201 mg, 55%) as a greenish oil as a 50:50 mixture of diastereomers. R_f = 0.25 (PE/EtOAc = 5:1); IR (neat) 3413, 1733, 1603, 1494, 1453, 1370, 1232, 1018, 964 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.27 (m, 10H), 6.22 (d, J = 6.4 Hz, 1H), 5.72 (m, 1H), 5.63 (ddd, J = 15.2, 6.4, and 0.8 Hz, 1H), 4.64 (dd, J = 7.2 and 5.6 Hz, 1H), 2.09 (s, 1.5H), 2.08 (s, 1.5H), 2.11−2.03 (m, 3H), 1.84−1.65 (m, 2H), 1.53 (m, 1H), 1.39 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 170.2, 144.9, [139.77 and 139.76], [134.4 and 134.3], [128.72 and 128.70], 128.6 (2C), 128.5 (2C), 128.0, [127.60 and 127.59], [127.0 (2C) and 126.9 (2C)], [126.0 (2C) and 125.9 (2C)], [76.37 and 76.36], [74.41 and 74.37], [38.54 and 38.53], [32.09 and 32.08], [25.1 and 25.0], 21.4; LRMS (EI) m/z (rel intensity) 264 ($[M - AcOH]^{\cdot+}$, 12), 130 (16), 129, (18), 117 (12), 115 (17), 105 (22), 104 ($[PhC_2H_3]^{\cdot+}$, 100), 91 (21), 77 ($[C_6H_5]^+$, 15); HRMS (ESI) calcd for $C_{21}H_{24}O_3Na$ $[M + Na]^+$ 347.1618, found 347.1618.

*(E)-7-Hydroxy-1,5,7-triphenylhept-2-en-1-yl Acetate (5,7-anti-isomer) (anti-**6**).* This compound was prepared according to GP2 using alcohol *anti*-**5** (200 mg, 0.79 mmol) and allylic acetate **S5**. The product was purified by column chromatography (pentane/Et_2O = 2:1) to furnish pure olefin *anti*-**6** (131 mg, 41%) as a colorless oil as a 50:50 mixture of diastereomers. R_f = 0.20 (PE/Et_2O = 2:1); IR (neat) 3436, 1731, 1602, 1493, 1454, 1371, 1234, 1018, 965 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36−7.19 (m, 14H), 7.15 (m, 1H), 6.15 (dd, J = 6.7 and 2.6 Hz, 1H), 5.69−5.49 (m, 2H), 4.37 (bd_{app}, J = 10.2 Hz, 1H), 3.07 (m, 1H), 2.44−2.32 (m, 2H), 2.09 (m, 1H), 2.07 (s, 1.5H), 2.04 (s, 1.5H), 1.90 (ddd, J = 14.3, 11.2, and 3.2 Hz, 1H), 1.85 (bs, 0.5H), 1.80 (bs, 0.5H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ [170.2 and 170.1], [145.4 and 145.3], [144.1 and 144.0], [139.6 and 139.5], [132.7 and 132.1], [130.1 and 130.0], [128.66 (2C) and 128.65 (2C)], 128.53 (3C), 128.48, [128.1 (2C) and 128.03 (2C)], [128.00 and 127.9], [127.52 and 127.51], [127.1 (2C) and 126.8 (2C)], 126.5, 125.6 (2C), [76.2 and 76.0], [71.87 and 71.86], [45.52 and 45.50], [42.5 and 42.3], [40.28 and 40.26], [21.5 and 21.4]; LRMS (EI) m/z (rel intensity) 340 ($[M - AcOH]^{\cdot+}$, 1), 193 (24), 131 (14), 130

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([PhC_4H_5]$^+$, 13), 129 (20), 115 (30), 105 ([PhCO]$^+$, 29), 104 ([PhC_2H_3]$^+$, 100), 103 (18), 91 (27), 78 (18), 77 ([C_6H_5]$^+$, 21); HRMS (ESI) calcd for $C_{27}H_{28}O_3Na$ [M + Na]$^+$ 423.1931, found 423.1929.

*(E)-7-Hydroxy-1,5,7-triphenylhept-2-en-1-yl Acetate (5,7-syn-isomer) (syn-**6**).* This compound was prepared according to GP2 using alcohol *syn*-**5** (161 mg, 0.64 mmol) and allylic acetate **S5**. The product was purified by column chromatography (pentane/EtOAc = 5:1) to furnish pure olefin *syn*-**6** (104 mg, 41%) as a colorless oil as a 50:50 mixture of diastereomers. R_f = 0.29 (PE/EtOAc = 5:1); IR (neat) 3413, 1733, 1602, 1493, 1453, 1370, 1232, 1060, 1018, 964 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.17 (m, 13H), 7.14−7.10 (m, 2H), 6.12 (bd, J = 5.3 Hz, 1H), 5.56−5.46 (m, 2H), 4.49 (bq_{app}, J = 7.0 Hz, 1H), 2.54 (m, 1H), 2.43−2.27 (m, 2H), 2.19 (m, 1H), 2.09 (m, 1H), 2.06 (s, 1.5H), 2.03 (s, 1.5H), 1.78 (bd, J = 2.7 Hz, 0.5H), 1.75 (d, J = 2.7 Hz, 0.5H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ [170.2 and 170.1], [144.31 and 144.29], [144.24 and 144.22], [139.6 and 139.4], [132.5 and 131.7], [130.3 and 130.2], 128.664 (3C), 128.656, [128.55 (2C) and 128.50 (2C)], [128.1 and 128.0], [127.94 and 127.90], [127.92 (2C) and 127.88 (2C)], 127.1, 126.8, [126.533 and 126.525], [126.46 (2C) and 126.43 (2C)], [76.2 and 75.9], [73.02 and 72.99], [44.63 and 44.57], [42.4 and 42.3], [40.00 and 39.97], [21.5 and 21.4]; LRMS (EI) m/z (rel intensity) 340 ([M − AcOH]$^{\cdot+}$, 2), 193 (27), 131 (17), 129 (18), 115 (29), 105 ([PhCO]$^+$, 23), 104 ([PhC_2H_3]$^{\cdot+}$, 100), 103 (18), 91 (20); HRMS (ESI) calcd for $C_{27}H_{28}O_3Na$ [M + Na]$^+$ 423.1931, found 423.1929

*(E)-5,7-Dihydroxy-1,7-diphenylhept-2-en-1-yl Acetate (5,7-anti-isomer) (anti-**11**).* This compound was prepared according to GP2 using alcohol *anti*-**10** (95 mg, 0.49 mmol) and allylic acetate **S5**. The product was purified by column chromatography (pentane/EtOAc = 3:2) to furnish pure olefin *anti*-**11** (50 mg, 30%) as a brownish oil as a 50:50 mixture of diastereomers. R_f = 0.24 (PE/EtOAc = 3:2); IR (neat) 3395, 1733, 1603, 1494, 1453, 1371, 1235, 1058, 1022, 968 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.24 (m, 10H), 6.19 (m, 1H), 5.74−5.71 (m, 2H), 5.03 (bdd, J = 8.1 and 3.1 Hz, 1H), 3.92 (bd_{app}, J = 6.1 Hz, 1H), 3.25 (bs, 0.5H), 3.21 (bs, 0.5H), 2.76 (bs, 0.5H), 2.73 (bs, 0.5H), 2.29−2.25 (m, 2H), 2.08 (s, 3H), 1.94−1.79 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ [170.4 and 170.3], [144.6 and 144.5], [139.4 and 139.3], [132.0 and 131.8], [130.1 and 129.8], 128.7 (2C), [128.55 (2C) and 128.53 (2C)], 128.2, [127.43 and 127.39], [127.0 (2C) and 126.9 (2C)], [125.62 (2C) and 125.60 (2C)], [76.5 and 76.2], [71.59 and 71.57], [68.2 and 68.1], [44.25 and 44.17], [40.5 and 40.4], [21.5 and 21.4]; LRMS (EI) m/z (rel intensity) 280 ([M − AcOH]$^{\cdot+}$, 1), 262 ([M − AcOH − H_2O]$^{\cdot+}$, 7), 131 (24), 130 ([PhC_4H_5]$^{\cdot+}$, 56), 129 (21), 115 (17), 105 ([PhCO]$^+$, 30), 104 ([PhC_2H_3]$^{\cdot+}$, 100), 103 (16), 92 (18), 91 (19), 78 (16), 77 ([C_6H_5]$^+$, 19); HRMS (ESI) calcd for $C_{21}H_{24}O_4Na$ [M + Na]$^+$ 363.1567, found 363.1567.

*(E)-5,7-Dihydroxy-1,7-diphenylhept-2-en-1-yl Acetate (5,7-syn-isomer) (syn-**11**).* This compound was prepared according to GP2 using alcohol *syn*-**10** (100 mg, 0.52 mmol) and allylic acetate **S5**. The product was purified by column chromatography (pentane/EtOAc = 3:2) to furnish pure olefin *syn*-**11** (60 mg, 34%) as a brownish oil as a 50:50 mixture of diastereomers. R_f = 0.35 (PE/EtOAc = 3:2); IR (neat) 3373, 1732, 1603, 1494, 1453, 1431, 1371, 1232, 1062, 1020, 967 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.27 (m, 10H), 6.21 (t_{app}, J = 4.9 Hz, 1H), 5.80−5.68 (m, 2H), 4.89 (dd, J = 9.1 and 4.1 Hz, 1H), 3.95 (m, 1H), 3.64 (bs, 0.5H), 3.62 (bs, 0.5H), 3.38 (bs, 0.5H), 3.36 (bs, 0.5H), 2.26−2.22 (m, 2H), 2.08 (s, 1.5H), 2.07 (s, 1.5H), 1.87−1.72 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ [170.4 and 170.3], [144.43 and 144.41], [139.38 and 139.37], [131.9 and 131.8], [129.8 and 129.7], [128.66 (2C) and 128.65 (2C)], [128.57 (2C) and 128.56 (2C)], 128.2, 127.7, [127.0 (2C) and 126.9 (2C)], [125.77 (2C) and 125.75 (2C)], [76.4 and 76.2], [75.05 and 75.00], [71.7 and 71.5], [44.93 and 44.90], [40.92 and 40.88], [21.45 and 21.42]; LRMS (EI) m/z (rel intensity) 156 (27), 131 (24), 130 ([PhC_4H_5]$^{\cdot+}$, 70), 129 (58), 128 (48), 127 (25), 115 (51), 106 (43), 105 ([PhCO]$^+$, 63), 104 ([PhC_2H_3]$^{\cdot+}$, 68), 103 (27), 91 (48), 78 (44), 77 ([C_6H_5]$^+$, 100), 76 (21), 74 (22), 65 (25), 64 (26), 63 (32), 52 (38), 51 (82), 50 (42); HRMS (ESI) calcd for $C_{21}H_{24}O_4Na$ [M + Na]$^+$ 363.1567, found 363.1567

*(E)-7-(2-Chloropyridin-3-yl)-7-hydroxy-1-phenylhept-2-en-1-yl Acetate (**17b**).* This compound was prepared according to GP2 using alcohol **16b** (360 mg, 1.70 mmol) and allylic acetate **S5**. The product was purified by column chromatography (PE/EtOAc = 3:2) to furnish pure olefin **17b** (334 mg, 55%) as a pale yellow oil as a 50:50 mixture of diastereomers. R_f = 0.44 (PE/EtOAc = 3:2); IR (neat) 3399, 1734, 1566, 1408, 1371, 1232, 1056, 1019, 965 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.27 (dd, J = 4.8 and 2.0 Hz, 1H), 7.90 (ddd, J = 7.6, 2.0, and 0.8 Hz, 1H), 7.36−7.25 (m, 6H), 6.20 (d, J = 6.4 Hz, 1H), 5.73 (m, 1H), 5.65 (ddd_{app}, J = 15.6, 6.4, and 0.8 Hz, 1H), 5.05 (m, 1H), 2.44 (d, J = 4.0 Hz, 0.5H), 2.41 (d, J = 4.0 Hz, 0.5H), 2.11 (bq_{app}, J = 6.8 Hz, 2H), 2.082 (s, 1.5H), 2.079 (s, 1.5H), 1.78 (m, 1H), 1.69−1.47 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ [170.34 and 170.27], [148.81 and 148.79], [148.31 and 148.30], [139.71 and 139.67], [139.2 and 139.1], [136.33 and 136.30], [134.2 and 134.1], [129.0 and 128.9], 128.6 (2C), [128.08 and 128.07], [126.97 (2C) and 126.96 (2C)], [123.04 and 123.03], [76.5 and 76.4], [69.9 and 69.8], 36.9, [31.91 and 31.88], [24.9 and 24.8], 21.5; LRMS (EI) m/z (rel intensity) 264 ([M − AcOH − Cl]$^+$, 6), 139 (14), 132 (18), 115 (17), 104 (100), 91 (14), 78 (14), 77 ([C_6H_5]$^+$, 20), 51 (17); HRMS (ESI) calcd for $C_{20}H_{22}ClNO_3Na$ [M + Na]$^+$ 382.1180, found 382.1185

*(E)-7-(4,6-Dichloropyrimidin-5-yl)-7-hydroxy-1-phenylhept-2-en-1-yl Acetate (**17c**).* This compound was prepared according to GP2 using alcohol **16c** (95 mg, 0.38 mmol) and allylic acetate **S5**. The product was purified by column chromatography (PE/EtOAc = 4:1) to furnish pure olefin **17c** (91 mg, 60%) as a yellow oil as a 50:50 mixture of diastereomers. R_f = 0.23 (PE/EtOAc = 4:1); IR (neat) 3434, 1732, 1533, 1515, 1416, 1370, 1331, 1232, 1019, 964 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.659 (s, 0.5H), 8.657 (s, 0.5H), 7.38−7.27 (m, 5H), 6.20 (d, J = 6.0 Hz, 1H), 5.76−5.63 (m, 2H), 5.29 (bs, 1H), 2.81 (bs, 1H, OH), 2.17−2.02 (m, 3H), 2.082 (s, 1.5H), 2.079 (s, 1.5H), 1.81 (m, 1H), 1.68 (m, 1H), 1.43 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ [170.3 and 170.2], 160.7 (2C), 156.4, [139.58 and 139.56], [133.7 and 133.5], [133.39 and 133.37], [129.4 and 129.3], 128.6 (2C), 128.1, [126.91 (2C) and 126.89 (2C)], [76.4 and 76.3], [70.2 and 70.1], [34.08 and 34.07], 31.7, [25.09 and 25.05], 21.5; LRMS (EI) m/z (rel intensity) 336 ([M − AcOH]$^{\cdot+}$, 1), 334 ([M − AcOH]$^{\cdot+}$, 1), 131 (12), 105 (10), 104 ([PhC_2H_3]$^{\cdot+}$, 100); HRMS (ESI) calcd for $C_{19}H_{20}Cl_2N_2O_3Na$ [M + Na]$^+$ 417.0743, found 417.0744.

*(E)-7-(1-Chloroisoquinolin-7-yl)-7-hydroxy-1-phenylhept-2-en-1-yl Acetate (**17d**).* This compound was prepared according to GP2 using alcohol **16d** (100 mg, 0.38 mmol) and allylic acetate **S5**. The product was purified by column chromatography (pentane/EtOAc = 2:1) to furnish pure olefin **17d** (76 mg, 49%) as a yellow oil as a 50:50 mixture of diastereomers. R_f = 0.50 (PE/EtOAc = 1:1); IR (neat) 3370, 1731, 1588, 1552, 1495, 1437, 1371, 1305, 1232, 1019, 995, 964 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.18 (bs, 1H), 8.18 (d, J = 5.6 Hz, 1H), 7.76 (dd, J = 8.8 and 1.6 Hz, 1H), 7.71 (ddd, J = 8.4, 3.2, and 1.6 Hz, 1H), 7.53 (d, J = 5.6 Hz, 1H), 7.34−7.24 (m, 5H), 6.18 (d, J = 6.8 Hz, 1H), 5.70 (dtd, J = 15.6, 6.0, and 2.4 Hz, 1H), 5.61 (dd, J = 15.2 and 6.4 Hz, 1H), 4.88 (bt, J = 6.0 Hz, 1H), 3.03 (bs, 1H, OH), 2.11−2.02 (m, 2H), 2.060 (s, 1.5H), 2.058 (s, 1.5H), 1.90−1.71 (m, 2H), 1.56 (m, 1H), 1.43 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 170.2, 151.5, 145.8, 141.3, 139.6, 137.2, [134.1 and 134.0], [129.7 and 129.6], 128.9, 128.6 (2C), 128.0, 127.4, [126.89 (2C) and 126.88 (2C)], 126.8, [122.83 and 122.81], 120.7, [76.4 and 76.3], [73.93 and 73.87], [38.6 and 38.5], [32.01 and 31.99], [25.0 and 24.9], 21.4; LRMS (EI) m/z (rel intensity) 351 ([M − AcOH]$^{\cdot+}$, 6), 349 ([M − AcOH]$^{\cdot+}$, 15), 245 (33), 219 (19), 217 (49), 191 ([1-chloroisoquinolineC_2H_3]$^{\cdot+}$, 37), 190 (17), 189 ([1-chloroisoquinolineC_2H_3]$^{\cdot+}$, 100), 154 (33), 130 (24), 129 ([isoquinoline]$^{\cdot+}$, 33), 128 ([isoquinoline − H]$^+$, 22), 127 ([isoquinoline − 2H]$^{\cdot+}$, 20), 115 (29), 104 ([PhC_2H_3]$^{\cdot+}$, 24), 91 (18), 77 ([C_6H_5]$^+$, 22); HRMS (ESI) calcd for $C_{24}H_{24}ClNO_3Na$ [M + Na]$^+$ 432.1337, found 432.1338.

*(E)-7-(2-Chloroquinolin-3-yl)-7-hydroxy-1-phenylhept-2-en-1-yl Acetate (**17e**).* This compound was prepared according to GP2 using alcohol **16e** (130 mg, 0.50 mmol) and allylic acetate **S5**. The product

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was purified by column chromatography (pentane/EtOAc = 3:1) to furnish pure olefin **17e** (105 mg, 52%) as a yellow oil as a 50:50 mixture of diastereomers. R_f = 0.32 (PE/EtOAc = 3:1); IR (neat) 3392, 1732, 1590, 1563, 1491, 1454, 1371, 1325, 1233, 1138, 1019, 961 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.31 (s, 1H), 7.98 (bd, J = 8.4 Hz, 1H), 7.78 (bd, J = 8.0 Hz, 1H), 7.69 (ddd, J = 8.4, 6.8, and 1.2 Hz, 1H), 7.53 (ddd, J = 8.0, 6.8, and 1.2 Hz, 1H), 7.35−7.21 (m, 5H), 6.19 (d, J = 6.4 Hz, 1H), 5.73 (m, 1H), 5.64 (dd, J = 15.2 and 6.4 Hz, 1H), 5.16 (m, 1H), 2.84 (bs, 1H, OH), 2.15−2.03 (m, 2H), 2.071 (s, 1.5H), 2.068 (s, 1.5H), 1.88 (m, 1H), 1.73−1.53 (m, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ [170.33 and 170.27], [148.81 and 148.80], 146.8, [139.7 and 139.6], 136.8, [135.74 and 135.72], [134.3 and 134.1], 130.3, [128.92 and 128.86], 128.6 (2C), 128.1, 128.0, [127.73 and 127.72], [127.49 and 127.48], 127.2, 126.9 (2C), [76.44 and 76.40], [70.2 and 70.1], [37.21 and 37.19], [31.91 and 31.89], [25.1 and 25.0], [21.49 and 21.48]; LRMS (EI) m/z (rel intensity) 314 ([M − AcOH-Cl]$^+$, 43), 216 (17), 210 (16), 201 (24), 191 ([2-chloroquinolineC_2H_3]$^{\cdot+}$, 33), 190 (15), 189 ([2-chloroquinolineC_2H_3]$^{\cdot+}$, 83), 182 (85), 181 (19), 167 (15), 155 (19), 154 (34), 153 (19), 141 (15), 131 (17), 130 ([PhC_4H_5]$^{\cdot+}$, 29), 129 ([quinoline]$^{\cdot+}$, 37), 128 ([quinoline − H]$^+$, 33), 127 ([quinoline − 2H]$^{\cdot+}$, 36), 115 (37), 105 (18), 104 ([PhC_2H_3]$^{\cdot+}$, 100), 103 (21), 91 (31), 78 (16), 77 ([C_6H_5]$^+$, 32), 75 (18), 51 (22); HRMS (ESI) calcd for $C_{24}H_{24}ClNO_3Na$ [M + Na]$^+$ 432.1337, found 432.1340.

*(E)-7-(2-Chloro-1-phenyl-1H-imidazol-5-yl)-7-hydroxy-1-phenylhept-2-en-1-yl Acetate (**17f**).* This compound was prepared according to GP2 using alcohol **16f** (95 mg, 0.34 mmol) and allylic acetate **S5**. The product was purified by column chromatography (PE/EtOAc = 1:1) to furnish pure olefin **17f** (74 mg, 51%) as a yellow oil as a 50:50 mixture of diastereomers. R_f = 0.27 (PE/EtOAc = 1:1); IR (neat) 3286, 1733, 1598, 1498, 1453, 1371, 1233, 1073, 1017, 965 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.49 (m, 3H), 7.36−7.27 (m, 7H), 6.96 (s, 1H), 6.18 (d, J = 6.0 Hz, 1H), 5.66 (dt, J = 15.2 and 6.0 Hz, 1H), 5.58 (dd, J = 15.2 and 6.4 Hz, 1H), 4.31 (bt, J = 6.4 Hz, 1H), 2.26 (bs, 1H, OH), 2.08 (s, 3H), 2.01 (q_{app}, J = 6.4 Hz, 2H), 1.72 (q_{app}, J = 7.6 Hz, 2H), 1.49 (m, 1H), 1.37 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ [170.21 and 170.19], [139.67 and 139.66], [137.70 and 137.68], 134.9, [133.9 and 133.8], 133.3, 129.8 (2C), 129.6 (2C), [129.01 and 128.99], 128.7, 128.6 (2C), [128.10 and 128.08], [126.93 (2C) and 126.89 (2C)], [125.47 and 125.45], 76.3, 65.0, [35.093 and 35.085], 31.8, [25.11 and 25.09], 21.5; LRMS (EI) m/z (rel intensity) 366 ([M − AcOH]$^{\cdot+}$, 9), 364 ([M − AcOH]$^{\cdot+}$, 20), 301 (15), 233 (18), 232 (17), 231 (55), 220 (19), 218 (18), 217 (21), 206 ([2-chloro-1-phenylimidazoleC_2H_3]$^{\cdot+}$, 32), 205 (37), 204 ([2-chloro-1-phenylimidazoleC_2H_3]$^{\cdot+}$, 88), 203 (36), 186 (24), 169 (31), 143 (18), 142 (34), 138 (19), 131 (27), 130 ([PhC_4H_5]$^{\cdot+}$, 100), 129 (84), 128 (39), 117 (18), 116 (29), 115 (68), 103 (19), 91 (31), 78 (27), 77 ([C_6H_5]$^+$, 84), 65 (20), 51 (34); HRMS (ESI) calcd for $C_{24}H_{25}ClN_2O_3Na$ [M + Na]$^+$ 447.1446, found 447.1446.

*(E)-7-(3-Chloro-1-methyl-1H-pyrazol-4-yl)-7-hydroxy-1-phenylhept-2-en-1-yl Acetate (**17g**).* This compound was prepared according to GP2 using alcohol **16g** (70 mg, 0.33 mmol) and allylic acetate **S5**. The product was purified by column chromatography (PE/EtOAc = 1:1) to furnish pure olefin **17g** (55 mg, 46%) as a greenish oil as a 50:50 mixture of diastereomers. R_f = 0.28 (PE/EtOAc = 1:1); IR (neat) 3395, 1731, 1557, 1494, 1407, 1371, 1233, 1071, 1018, 965 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36−7.27 (m, 5H), 7.26 (s, 1H), 6.20 (d, J = 6.4 Hz, 1H), 5.71 (dtd, J = 15.2, 6.0, and 1.6 Hz, 1H), 5.63 (dd, J = 15.2 and 6.4 Hz, 1H), 4.64 (t, J = 6.8 Hz, 1H), 3.79 (s, 3H), 2.28 (bs, 1H, OH), 2.11−2.06 (m, 2H), 2.079 (s, 1.5H), 2.076 (s, 1.5H), 1.82−1.66 (m, 2H), 1.52 (m, 1H), 1.39 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ [170.23 and 170.20], [139.713 and 139.705], 136.6, [134.2 and 134.1], [129.61 and 129.59], 128.8, 128.6 (2C), 128.0, [126.93 (2C) and 126.92 (2C)], [122.28 and 122.27], [76.38 and 76.35], [65.48 and 65.45], 39.6, [37.04 and 37.02], 31.9, [24.90 and 24.86], [21.46 and 21.45]; LRMS (EI) m/z (rel intensity) 304 ([M − AcOH]$^{\cdot+}$, 3), 302 ([M − AcOH]$^{\cdot+}$, 8), 267 ([M − AcOH-Cl]$^+$, 17), 155 (19), 144 ([3-chloro-1-methylpyrazoleC_2H_3]$^{\cdot+}$, 29), 143 (19), 142 ([3-chloro-1-methylpyrazoleC_2H_3]$^{\cdot+}$, 100), 135 (29), 131 (17), 130 ([PhC_4H_5]$^{\cdot+}$, 36), 129 (46), 128 (20), 115 ([3-chloro-1-methylpyrazole-H]$^+$, 30), 91 (25), 77 ([C_6H_5]$^+$, 17). HRMS (ESI) calcd for $C_{19}H_{23}ClN_2O_3Na$ [M + Na]$^+$ 385.1289, found 385.1292.

*(E)-7-(1-Acetyl-1H-indol-3-yl)-7-hydroxy-1-phenylhept-2-en-1-yl Acetate (**17h**).* This compound was prepared according to GP2 using alcohol **16h** (100 mg, 0.39 mmol) and allylic acetate **S5**. The product was purified by column chromatography (PE/EtOAc = 2:1) to furnish pure olefin **17h** (72 mg, 46%) as a pale yellow oil as a 50:50 mixture of diastereomers. R_f = 0.29 (PE/EtOAc = 2:1); IR (neat) 3436, 1732, 1704, 1605, 1450, 1371, 1329, 1233, 1123, 1017, 964 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.43 (bd, J = 8.4 Hz, 1H), 7.62 (dddd, J = 7.6, 2.8, 1.2, and 0.8 Hz, 1H), 7.38−7.27 (m, 8H), 6.20 (d, J = 6.4 Hz, 1H), 5.73 (dtd, J = 15.2, 6.4, and 1.6 Hz, 1H), 5.64 (ddd, J = 15.2, 6.4, and 0.8 Hz, 1H), 4.96 (bt, J = 6.4 Hz, 1H), 2.57 (s, 3H), 2.15−2.04 (m, 3H), 2.08 (s, 1.5H), 2.07 (s, 1.5H), 1.96−1.88 (m, 2H), 1.61 (m, 1H), 1.50 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ [170.23 and 170.22], [168.80 and 168.78], 139.7, 136.4, [134.22 and 134.16], 128.9, 128.6 (2C), 128.1, 127.0 (2C), [126.7 and 126.6], [126.13 and 126.12], 125.6, 123.7, [121.79 and 121.78], [119.78 and 119.75], [116.93 and 116.91], [76.39 and 76.37], [68.0 and 67.9], [36.82 and 36.81], 32.1, [25.09 and 25.05], 24.1, 21.5; LRMS (EI) m/z (rel intensity) 345 ([M − AcOH]$^{\cdot+}$, 6), 144 (19), 143 (61), 130 ([PhC_4H_5]$^{\cdot+}$, 100), 129 (33), 128 (22), 117 (20), 115 ([indole − H]$^{\cdot+}$, 44), 91 (22), 77 ([C_6H_5]$^+$, 19); HRMS (ESI) calcd for $C_{25}H_{27}NO_4Na$ [M + Na]$^+$ 428.1832, found 428.1833.

*(E)-7-Hydroxy-1-phenyl-7-(1-tosyl-1H-pyrrol-2-yl)hept-2-en-1-yl Acetate (**17i**).* This compound was prepared according to GP2 using alcohol **16i** (150 mg, 0.47 mmol) and allylic acetate **S5**. The product was purified by column chromatography (pentane/EtOAc = 3:1) to furnish pure olefin **17i** (121 mg, 55%) as a yellow oil as a 50:50 mixture of diastereomers. R_f = 0.35 (PE/EtOAc = 3:1); IR (neat) 3555, 1732, 1597, 1453, 1366, 1234, 1173, 1149, 1089, 1056, 1018, 965, 909 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.64 (dt_{app}, J = 8.4 and 2.0 Hz, 2H), 7.34−7.23 (m, 8H), 6.23−6.21 (m, 2H), 6.19 (bd, J = 6.8 Hz, 1H), 5.67 (dtd, J = 15.6, 6.4, and 1.6 Hz, 1H), 5.57 (ddd, J = 15.2, 6.4, and 0.8 Hz, 1H), 4.78 (m, 1H), 2.83 (bd, J = 3.6 Hz, 1H, OH), 2.35 (s, 3H), 2.063 (s, 1.5H), 2.057 (s, 1.5H), 2.04−1.91 (m, 2H), 1.84−1.69 (m, 2H), 1.48 (m, 1H), 1.35 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 170.1, 145.2, [139.70 and 139.68], [138.10 and 138.08], 136.3, [134.2 and 134.1], 130.1 (2C), 128.7, 128.5 (2C), [127.97 and 127.96], [126.90 (2C) and 126.87 (2C)], 126.6 (2C), 123.4, [112.31 and 112.30], [111.614 and 111.606], [76.24 and 76.23], 65.0, [34.62 and 34.60], 31.8, [25.33 and 25.32], 21.6, [21.42 and 21.41]; LRMS (EI) m/z (rel intensity) 407 ([M − AcOH]$^{\cdot+}$, 5), 389 ([M − AcOH-H_2O]$^{\cdot+}$, 4), 252 ([M − AcOH − pTolSO$_2$]$^{\cdot+}$, 40), 155 ([pTolSO$_2$]$^+$, 20), 148 (16), 130 ([PhC_4H_5]$^{\cdot+}$, 59), 129 (23), 128 (19), 115 (23), 106 (30), 92 (16), 91 ([pTol]$^+$, 100), 80 (22), 65 ([pyrrole − H]$^{\cdot+}$, 29); HRMS (ESI) calcd for $C_{26}H_{29}NO_5SNa$ [M + Na]$^+$ 490.1659, found 490.1658

*(E)-1-(4-Chloro-7-(phenylsulfonyl)-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-7-hydroxy-7-phenylhept-2-en-1-yl Acetate (**17j**).* This compound was prepared according to GP2 using alcohol **16j** (135 mg, 0.77 mmol, 3.0 equiv) and allylic acetate **19** (100 mg, 0.26 mmol, 1.0 equiv). The product was purified by column chromatography (PE/EtOAc = 2:1) to furnish pure olefin **17j** (40 mg, 29%) as a colorless oil as a 50:50 mixture of diastereomers. R_f = 0.41 (PE/EtOAc = 1:1); IR (neat) 3418, 1740, 1583, 1538, 1449, 1436, 1386, 1230, 1188, 1155, 1091, 1014, 909 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.74 (s, 1H), 8.23 (dd, J = 8.4 and 1.6 Hz, 2H), 7.76 (d, J = 1.2 Hz, 1H), 7.66 (tt_{app}, J = 7.2 and 1.6 Hz, 1H), 7.55 (tt_{app}, J = 8.4 and 1.6 Hz, 2H), 7.37−7.27 (m, 5H), 6.65 (d, J = 6.8 Hz, 1H), 5.82 (dt, J = 15.6 and 6.4 Hz, 1H), 5.70 (ddt, J = 15.6, 6.8, and 1.2 Hz, 1H), 4.68 (dd, J = 7.6 and 5.6 Hz, 1H), 2.14 (m, 1H), 2.10 (s, 1.5H), 2.09 (s, 1.5H), 1.85−1.67 (m, 4H), 1.56 (m, 1H), 1.41 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 169.8, 153.0, 152.8, 151.7, 144.8, 137.3, [136.75 and 136.74], 135.2, 129.5 (2C), 128.7 (2C), 128.6 (2C), [127.734 and 127.726], [126.15 and 126.13], [125.97 (2C) and 125.95 (2C)], 125.5, 117.62, 117.56, [74.50 and 74.48], [68.67 and 68.66], [38.60 and 38.58], 32.1, [25.02 and 25.00], 21.4; LRMS (EI) m/z (rel intensity) not detected by GC-MS; HRMS (ESI) calcd for $C_{27}H_{26}ClN_3O_5SNa$ [M + Na]$^+$ 562.1174, found 562.1174.

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General Procedure 3 (GP3). *Iron-Catalyzed Cyclization of Allylic Acetates.* To a stirred solution of allylic acetate (1.0 equiv) in CH_2Cl_2 (0.1 M) was added powdered $FeCl_3{\cdot}6H_2O$ (5 mol %), and the mixture was stirred at rt. The solution was then filtered through a pad of silica gel (pentane/EtOAc = 3:1), and the solvents were removed under reduced pressure to yield the corresponding oxygen heterocycle.

*(E)-2-Phenyl-6-styryltetrahydro-2H-pyran (**4**).* This compound was prepared according to GP3 using allylic acetate **3** (45 mg, 0.14 mmol). After 2 h, pure *cis*-tetrahydropyran **4** was isolated (33 mg, 90%) as a colorless oil. R_f = 0.58 (PE/EtOAc = 10:1); IR (neat) 1600, 1493, 1450, 1300, 1190, 1070, 1039, 964 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.46−7.40 (m, 4H), 7.39−7.35 (m, 2H), 7.34−7.30 (m, 2H), 7.28 (tt, J = 7.6 and 1.6 Hz, 1H), 7.24 (tt, J = 7.2 and 1.2 Hz, 1H), 6.67 (dd, J = 16.0 and 1.2 Hz, 1H), 6.34 (dd, J = 16.0 and 6.0 Hz, 1H), 4.51 (dd, J = 11.2 and 2.4 Hz, 1H), 4.24 (ddt_{app}, J = 11.2, 5.6, and 1.6 Hz, 1H), 2.04 (m, 1H), 1.92−1.75 (m, 3H), 1.65−1.50 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 143.4, 137.2, 131.1, 129.8, 128.6 (2C), 128.4 (2C), 127.5, 127.4, 126.6 (2C), 126.1 (2C), 80.1, 78.7, 33.7, 31.8, 24.2; LRMS (EI) m/z (rel intensity) 264 ($[M]^{\cdot+}$, 15), 130 ($[PhC_4H_5]^{\cdot+}$, 17), 129 (19), 115 (18), 105 (22), 104 ($[PhC_2H_3]^{\cdot+}$, 100), 91 (23), 77 ($[C_6H_5]^+$, 15); HRMS (ESI) calcd for $C_{19}H_{20}ONa$ $[M + Na]^+$ 287.1406, found 287.1407.

*2,4-Diphenyl-6-((E)-styryl)tetrahydro-2H-pyran (**7a**).* This compound was prepared according to GP3 using allylic acetate *anti*-**6** (60 mg, 0.15 mmol). After 1 h, pure *cis*-tetrahydropyran **7a** was isolated (42 mg, 82%) as a colorless oil. R_f = 0.45 (PE/EtOAc = 20:1); IR (neat) 1601, 1494, 1450, 1302, 1168, 1120, 1063, 1029, 964 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.49−7.47 (m, 2H), 7.43−7.22 (m, 13H), 6.73 (dd, J = 16.1 and 1.4 Hz, 1H), 6.38 (dd, J = 16.1 and 5.7 Hz, 1H), 4.68 (dd, J = 11.2 and 2.3 Hz, 1H), 4.41 (ddt_{app}, J = 11.2, 5.6, and 1.7 Hz, 1H), 3.11 (tt_{app}, J = 12.3 and 3.7 Hz, 1H), 2.17−2.07 (m, 2H), 1.85−1.71 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 145.3, 142.8, 137.1, 130.4, 130.2, 128.7 (2C), 128.6 (2C), 128.5 (2C), 127.63, 127.57, 126.9 (2C), 126.61 (2C), 126.60, 126.1 (2C), 79.8, 78.4, 42.2, 41.1, 39.2; LRMS (EI) m/z (rel intensity) 340 ($[M]^{\cdot+}$, 1), 193 (21), 131 (12), 130 ($[PhC_4H_5]^{\cdot+}$, 12), 129 (16), 115 (28), 105 ($[PhCO]^+$, 21), 104 ($[PhC_2H_3]^{\cdot+}$, 100), 103 (18), 91 (25), 78 (20), 77 ($[C_6H_5]^+$, 19); HRMS (ESI) calcd for $C_{25}H_{25}O$ $[M + H]^+$ 341.1900, found 341.1900.

*2,4-Diphenyl-6-((E)-styryl)tetrahydro-2H-pyran (**7b** and **7c**).* This compound was prepared according to GP3 using allylic acetate *syn*-**6** (60 mg, 0.15 mmol). After 48 h, a 65:35 mixture of 2,6-*trans*-tetrahydropyran **7b** and 2,6-*cis*-tetrahydropyran **7c** was isolated (33 mg, 65%) as a colorless oil. R_f = 0.73 (PE/EtOAc = 20:1); IR (neat) 1601, 1494, 1448, 1337, 1267, 1206, 1156, 1095, 1065, 1029 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.58−7.22 (m, 15H), 6.68 (dd, J = 16.1 and 1.5 Hz, 1H, **7b** and **7c**), 6.34 (dd, J = 16.0 and 6.0 Hz, 0.35H, **7c**), 6.31 (dd, J = 16.0 and 5.6 Hz, 0.65H, **7b**), 5.40 (d, J = 5.4 Hz, 0.65H, **7b**), 4.77 (dd, J = 11.5 and 2.4 Hz, 0.35H, **7c**), 4.49 (ddt_{app}, J = 11.6, 5.8, and 1.6 Hz, 0.35H, **7c**), 4.32 (ddt_{app}, J = 11.3, 5.4, and 1.7 Hz, 0.65H, **7b**), 3.51 (bs, 0.35H, **7c**) 3.01 (tt_{app}, J = 12.5 and 3.4 Hz, 0.65H, **7b**), 2.61 (ddt_{app}, J = 13.9, 3.5, and 1.8 Hz, 0.65H, **7b**), 2.46−2.36 (m, 0.70H, **7c**), 2.30 (ddd, J = 14.0, 12.8, and 5.6 Hz, 0.65H, **7b**), 2.21−2.08 (m, 0.70H, **7c**), 1.93 (m, 0.65H, **7b**), 1.79 (q_{app}, J = 12.1 Hz, 0.65H, **7b**); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 145.6 (**7b**), 143.4 (**7c**), 143.2 (**7c**), 140.4 (**7b**), 137.1 (**7c**), 137.0 (**7b**), 130.8 (**7c**), 130.5 (**7b**), 130.2 (**7c**), 130.1 (**7b**), 128.9 (2C, **7b**), 128.8 (2C, **7b**), 128.74 (2C, **7c**), 128.65 (2C, **7b**), 128.6 (2C, **7c**), 128.5 (2C, **7c**), 127.9 (**7b**), 127.7 (**7b**), 127.6 (**7c**), 127.5 (**7c**), 127.1 (2C, **7c**), 126.9 (2C, **7b**), 126.8 (2C, **7b**), 126.62 (2C, **7c**), 126.59 (2C, **7c**), 126.57 (2C, **7b**), 126.1 (**7b** and **7c**), 75.2 (**7c**), 74.1 (**7c**), 73.9 (**7b**), 70.9 (**7b**), 39.7 (**7b**), 37.6 (**7c**), 36.6 (**7b**), 35.7 (**7c**), 35.3 (**7c**), 33.9 (**7b**). LRMS (EI) m/z (rel intensity) 340 ($[M]^{\cdot+}$, 2), 193 (25), 145 (11), 131 (17), 130 ($[PhC_4H_5]^{\cdot+}$, 16), 129 (19), 115 (27), 105 ($[PhCO]^+$, 21), 104 ($[PhC_2H_3]^{\cdot+}$, 100), 103 (15), 91 (18), 78 (14), 77 ($[C_6H_5]^+$, 14); HRMS (ESI) calcd for $C_{25}H_{25}O$ $[M + H]^+$ 341.1900, found 341.1900.

*(E)-1,3,7-Triphenylhept-6-en-1-one (**8**).* To a stirred solution of a 65:35 mixture of tetrahydropyrans **7b** and **7c** (30 mg, 0.088 mmol, 1.0 equiv) in CH_2Cl_2 (1 mL) was added powdered $FeCl_3{\cdot}6H_2O$ (1.2 mg, 0.004 mmol, 0.05 equiv), and the mixture was stirred at 50 °C for 4 h. The solvent was removed under reduced pressure to give an orange oil, which was purified by column chromatography (pentane/EtOAc = 20:1) to yield ketone **8** (19 mg, 63%) as a colorless oil. R_f = 0.41 (PE/EtOAc = 20:1); IR (neat) 1683, 1597, 1580, 1494, 1449, 1366, 1269, 1204, 1180, 1073, 1026, 1001, 965 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.93−7.90 (m, 2H), 7.54 (tt_{app}, J = 7.2 and 1.2 Hz, 1H), 7.43 (tt_{app}, J = 8.0 and 1.6 Hz, 2H), 7.34−7.25 (m, 8H), 7.23−7.16 (m, 2H), 6.30 (bdt, J = 15.9 and 1.4 Hz, 1H), 6.16 (dt, J = 15.9 and 6.7 Hz, 1H), 3.42 (m, 1H), 3.33 (dd, J = 16.5 and 6.2 Hz, 1H), 3.28 (dd, J = 16.3 and 7.8 Hz, 1H), 2.15−2.05 (m, 2H), 1.96 (m, 1H), 1.82 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 199.1, 144.5, 137.9, 137.3, 133.1, 130.4, 130.3, 128.69 (2C), 128.68 (2C), 128.6 (2C), 128.2 (2C), 127.8 (2C), 127.0, 126.6, 126.1 (2C), 46.1, 41.0, 35.9, 31.0; LRMS (EI) m/z (rel intensity) 220 (17), 209 (21), 129 (42), 117 (16), 115 (25), 105 ($[PhCO]^+$, 100), 92 (21), 91 (38), 77 ($[C_6H_5]^+$, 64), 51 (15); HRMS (ESI) calcd for $C_{25}H_{24}ONa$ $[M + Na]^+$ 363.1719, found 363.1716.

*2-Phenyl-6-((E)-styryl)tetrahydro-2H-pyran-4-ol (**12a**).* This compound was prepared according to GP3 using allylic acetate *anti*-**11** (35 mg, 0.10 mmol). After 24 h, pure *cis*-tetrahydropyranol **12a** was isolated (25 mg, 87%) as a colorless oil. R_f = 0.39 (PE/EtOAc = 3:2); IR (neat) 3358, 1600, 1495, 1449, 1359, 1304, 1265, 1207, 1163, 1060, 965 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.42−7.20 (m, 10H), 6.66 (dd, J = 16.0 and 1.5 Hz, 1H), 6.29 (dd, J = 16.0 and 5.9 Hz, 1H), 4.47 (dd, J = 11.2 and 2.3 Hz, 1H), 4.20 (ddt_{app}, J = 11.4, 5.9, and 1.8 Hz, 1H), 4.04 (tt_{app}, J = 11.0 and 4.6 Hz, 1H), 2.25−2.15 (m, 2H), 1.76 (bs, 1H), 1.60−1.43 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 141.9, 136.9, 130.6, 129.6, 128.64 (2C), 128.55 (2C), 127.77, 127.76, 126.6 (2C), 126.2 (2C), 77.9, 76.5, 68.5, 43.0, 41.2; LRMS (EI) m/z (rel intensity) 262 ($[M - H_2O]^{\cdot+}$, 7), 131 (22), 130 ($[PhC_4H_5]^{\cdot+}$, 50), 129 (19), 115 (15), 105 ($[PhCO]^+$, 23), 104 ($[PhC_2H_3]^{\cdot+}$, 100), 92 (15), 91 (16), 78 (15), 77 ($[C_6H_5]^+$, 17); HRMS (ESI) calcd for $C_{19}H_{20}O_2Na$ $[M + Na]^+$ 303.1356, found 303.1355.

*2-Phenyl-6-((E)-styryl)tetrahydro-2H-pyran-4-ol (**12b**).* This compound was prepared according to GP3 using allylic acetate *syn*-**11** (40 mg, 0.12 mmol). After 48 h, pure 2,6-*cis*-tetrahydropyranol **12b** was isolated (31 mg, 94%) as a colorless oil. R_f = 0.53 (PE/EtOAc = 3:2); IR (neat) 3412, 1600, 1495, 1450, 1305, 1210, 1177, 1057, 965 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.43−7.19 (m, 10H), 6.66 (d, J = 15.9 Hz, 1H), 6.27 (dd, J = 16.0 and 6.0 Hz, 1H), 4.97 (dd, J = 11.6 and 2.6 Hz, 1H), 4.68 (m, 1H), 4.38 ($bquint_{app}$, J = 2.8 Hz, 1H), 1.95−1.74 (m, 4H), 1.72 (bs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 142.8, 137.1, 130.5, 130.3, 128.6 (2C), 128.5 (2C), 127.6, 127.5, 126.6 (2C), 126.2 (2C), 73.9, 72.8, 64.9, 40.5, 38.8; LRMS (EI) m/z (rel intensity) 280 ($[M]^{\cdot+}$, 2), 262 ($[M - H_2O]^{\cdot+}$, 8), 131 (21), 130 ($[PhC_4H_5]^{\cdot+}$, 52), 129 (18), 115 (13), 105 ($[PhCO]^+$, 23), 104 ($[PhC_2H_3]^{\cdot+}$, 100), 103 (12), 92 (13), 91 (12), 78 (12), 77 ($[C_6H_5]^+$, 13); HRMS (ESI) calcd for $C_{19}H_{21}O_2$ $[M + H]^+$ 281.1536, found 281.1538.

*(E)-2-Chloro-3-(6-styryltetrahydro-2H-pyran-2-yl)pyridine (**18b**).* This compound was prepared according to GP3 using allylic acetate **17b** (380 mg, 1.06 mmol). After 5 days, pure *cis*-tetrahydropyran **18b** was isolated (255 mg, 81%) as a yellow oil. R_f = 0.64 (PE/EtOAc = 4:1); IR (neat) 1598, 1582, 1564, 1494, 1447, 1412, 1377, 1200, 1187, 1070, 1039, 965 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.30 (dd, J = 4.8 and 1.2 Hz, 1H), 8.00 (ddd, J = 7.6, 1.2, and 0.8 Hz, 1H), 7.40 (bd, J = 7.6 Hz, 2H), 7.32 (bt, J = 7.2 Hz, 2H), 7.28 (dd, J = 7.6 and 3.6 Hz, 1H), 7.24 (bt, J = 8.0 Hz, 1H), 6.65 (d, J = 16.0 Hz, 1H), 6.29 (dd, J = 16.0 and 6.0 Hz, 1H), 4.80 (bd, J = 11.2 Hz, 1H), 4.26 (dd, J = 11.6 and 6.0 Hz, 1H), 2.11 (bd, J = 12.8 Hz, 1H), 2.02 (m, 1H), 1.89−1.77 (m, 2H), 1.54 (qd_{app}, J = 13.2 and 3.2 Hz, 1H), 1.30 (qd_{app}, J = 12.4 and 3.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 148.5, 148.2, 137.9, 137.0, 136.6, 130.4, 130.2, 128.6 (2C), 127.7, 126.6 (2C), 123.1, 78.8, 76.1, 32.1, 31.7, 23.9; LRMS (EI) m/z (rel intensity) 299 ($[M]^{\cdot+}$, 1), 264 ($[M - Cl]^+$, 9), 139 (10), 132 (17), 131 (10), 129 (10), 105 (11), 104 (100), 77 (11); HRMS (ESI) calcd for $C_{18}H_{19}ClNO$ $[M + H]^+$ 300.1150, found 300.1151

*(E)-4,6-Dichloro-5-(6-styryltetrahydro-2H-pyran-2-yl)pyrimidine (**18c**).* This compound was prepared according to GP3 using allylic acetate **17c** (40 mg, 0.10 mmol). After 5 days, pure *cis*-tetrahydropyran

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18c was isolated (31 mg, 91%) as a colorless oil. R_f = 0.56 (PE/EtOAc = 4:1); IR (neat) 1599, 1538, 1514, 1495, 1415, 1386, 1342, 1327, 1231, 1201, 1084, 1037, 965 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.67 (s, 1H), 7.40−7.37 (m, 2H), 7.32−7.28 (m, 2H), 7.22 (tt, J = 7.2 and 1.6 Hz, 1H), 6.68 (dd, J = 16.0 and, 1.2 Hz, 1H), 6.27 (dd, J = 16.0 and 6.0 Hz, 1H), 5.17 (dd, J = 11.6 and 2.4 Hz, 1H), 4.19 (ddt_{app}, J = 11.6, 6.0, and 1.6 Hz, 1H), 2.18 (qd_{app}, J = 12.1 and 4.0 Hz, 1H), 2.09 (m, 1H), 1.85−1.73 (m, 2H), 1.71−1.58 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 161.2 (2C), 156.4, 136.8, 132.1, 130.5, 129.8, 128.6 (2C), 127.7, 126.6 (2C), 79.1, 75.6, 31.4, 26.9, 23.6; LRMS (EI) m/z (rel intensity) 336 ($[M]^{\cdot+}$, 1), 334 ($[M]^{\cdot+}$, 2), 131 (15), 105 (10), 104 ($[PhC_2H_3]^{\cdot+}$, 100); HRMS (ESI) calcd for $C_{17}H_{17}Cl_2N_2O$ $[M + H]^+$ 335.0713, found 335.0714.

*(E)-1-Chloro-7-(6-styryltetrahydro-2H-pyran-2-yl)isoquinoline (**18d**).* This compound was prepared according to GP3 using allylic acetate **17d** (51 mg, 0.12 mmol). After 5 days, pure *cis*-tetrahydropyran **18d** was isolated (36 mg, 83%) as a colorless oil. R_f = 0.39 (CH_2Cl_2); IR (neat) 1588, 1551, 1496, 1438, 1380, 1308, 1284, 1257, 1202, 1164, 1080, 1039, 995 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.33 (bs, 1H), 8.25 (d, J = 5.6 Hz, 1H), 7.87 (dd, J = 8.8 and 1.6 Hz, 1H), 7.83 (bd, J = 8.4 Hz, 1H), 7.58 (dd, J = 5.6 and 0.8 Hz, 1H), 7.42 (dd, J = 8.4 and 1.6 Hz, 2H), 7.34−7.29 (m, 2H), 7.23 (tt, J = 7.2 and 1.2 Hz, 1H), 6.70 (dd, J = 16.0 and 1.2 Hz, 1H), 6.35 (dd, J = 16.0 and 5.6 Hz, 1H), 4.72 (dd, J = 11.6 and 2.4 Hz, 1H), 4.29 (ddt_{app}, J = 11.2, 6.0, and 1.6 Hz, 1H), 2.08 (m, 1H), 1.99 (m, 1H), 1.92−1.80 (m, 2H), 1.69−1.54 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 151.7, 144.1, 141.4, 137.3, 137.0, 130.6, 130.1, 130.0, 128.6 (2C), 127.7, 127.3, 127.0, 126.6 (2C), 123.1, 120.7, 79.6, 78.9, 33.7, 31.7, 24.1; LRMS (EI) m/z (rel intensity) 351 ($[M]^{\cdot+}$, 4), 349 ($[M]^{\cdot+}$, 13), 314 ($[M - Cl]^+$, 2), 245 (31), 219 (16), 217 (48), 191 ($[1\text{-chloroisoquinolineC}_2H_3]^{\cdot+}$, 36), 190 (20), 189 ($[1\text{-chloroisoquinolineC}_2H_3]^{\cdot+}$, 100), 154 (29), 130 (23), 129 ($[isoquinoline]^{\cdot+}$, 32), 128 ($[isoquinoline - H]^+$, 26), 127 ($[isoquinoline - 2H]^{\cdot+}$, 20), 115 (29), 104 ($[PhC_2H_3]^{\cdot+}$, 21), 91 (24), 77 ($[C_6H_5]^+$, 22); HRMS (ESI) calcd for $C_{22}H_{21}ClNO$ $[M + H]^+$ 350.1306, found 350.1306.

*(E)-2-Chloro-3-(6-styryltetrahydro-2H-pyran-2-yl)quinoline (**18e**).* This compound was prepared according to GP3 using allylic acetate **17e** (45 mg, 0.11 mmol). After 5 days, pure *cis*-tetrahydropyran **18e** was isolated (29 mg, 76%) as a colorless oil. R_f = 0.52 (PE/Et_2O = 4:1); IR (neat) 1620, 1592, 1490, 1449, 1371, 1330, 1310, 1197, 1139, 1078, 1052, 1031, 963 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.42 (s, 1H), 8.01 (ddd, J = 8.4, 2.0, and 0.8 Hz, 1H), 7.87 (ddd, J = 8.0, 0.8, and 0.4 Hz, 1H), 7.70 (ddd, J = 8.4, 6.8, and 1.2 Hz, 1H), 7.55 (ddd, J = 8.4, 7.2, and 1.2 Hz, 1H), 7.45−7.42 (m, 2H), 7.35−7.31 (m, 2H), 7.25 (tt, J = 7.2 and 1.2 Hz, 1H), 6.70 (dd, J = 16.0 and 1.2 Hz, 1H), 6.36 (dd, J = 16.0 and 6.0 Hz, 1H), 4.93 (dd, J = 10.8 and 2.0 Hz, 1H), 4.33 (ddt_{app}, J = 11.2, 6.0, and 1.6 Hz, 1H), 2.25 (m, 1H), 2.06 (m, 1H), 1.94−1.82 (m, 2H), 1.60 (m, 1H), 1.38 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 148.6, 146.9, 137.0, 136.0, 135.4, 130.5, 130.4, 130.2, 128.7 (2C), 128.3, 127.9, 127.78, 127.75, 127.1, 126.7 (2C), 79.2, 76.5, 32.8, 31.7, 24.0; LRMS (EI) m/z (rel intensity) 314 ($[M - Cl]^+$, 44), 191 ($[2\text{-chloroquinolineC}_2H_3]^{\cdot+}$, 42), 189 ($[2\text{-chloroquinolineC}_2H_3]^{\cdot+}$, 76), 182 (100), 154 (46), 129 ($[quinoline]^{\cdot+}$, 42), 128 ($[quinoline - H]^+$, 39), 127 ($[quinoline - 2H]^{\cdot+}$, 51), 115 (51), 104 ($[PhC_2H_3]^{\cdot+}$, 87), 91 (36), 77 ($[C_6H_5]^+$, 46); HRMS (ESI) calcd for $C_{22}H_{21}ClNO$ $[M + H]^+$ 350.1306, found 350.1307.

*(E)-2-Chloro-1-phenyl-5-(6-styryltetrahydro-2H-pyran-2-yl)-1H-imidazole (**18f**).* This compound was prepared according to GP3 using allylic acetate **17f** (80 mg, 0.19 mmol). After 18 days, pure *cis*-tetrahydropyran **18f** was isolated (39 mg, 57%) as white crystals. R_f = 0.39 (PE/EtOAc = 3:1); mp 132−134 °C; IR (neat) 1598, 1498, 1449, 1406, 1373, 1273, 1074, 1044, 1029, 966 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.49−4.47 (m, 3H), 7.47−7.29 (m, 6H), 7.23 (tt, J = 7.2 and 1.6 Hz, 1H), 7.07 (d, J = 0.8 Hz, 1H), 6.41 (dd, J = 16.0 and 1.2 Hz, 1H), 6.10 (dd, J = 16.0 and 6.0 Hz, 1H), 4.08 (m, 1H), 3.75 (ddt_{app}, J = 11.2, 6.0, and 1.6 Hz, 1H), 1.97 (ddt_{app}, J = 13.2, 6.0, and 3.2 Hz, 1H), 1.86−1.77 (m, 2H), 1.68 (dq_{app}, J = 12.8 and 2.8 Hz, 1H), 1.57 (m, 1H), 1.43 (tdd_{app}, J = 12.8, 10.8, and 4.0 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 136.9, 135.5, 135.2, 133.4, 130.4, 130.0, 129.4 (2C), 129.2 (2C), 128.7 (2C), 128.2, 127.7, 126.5 (2C), 126.2, 78.4, 70.8, 31.2, 28.4, 23.7; LRMS (EI) m/z (rel intensity) 231 (31), 206 ($[2\text{-chloro-1-phenylimidazoleC}_2H_3]^{\cdot+}$, 26), 205 (16), 204 ($[2\text{-chloro-1-phenylimidazoleC}_2H_3]^{\cdot+}$, 64), 203 (32), 142 (24), 130 ($[PhC_4H_5]^{\cdot+}$, 100), 129 (59), 128 (33), 116 (22), 115 (49), 91 (30), 78 (31), 77 ($[C_6H_5]^+$, 77), 51 (39); HRMS (ESI) calcd for $C_{22}H_{21}ClN_2O$ $[M + H]^+$ 365.1415, found 365.1416.

*(E)-3-Chloro-1-methyl-4-(6-styryltetrahydro-2H-pyran-2-yl)-1H-pyrazole (**18g**).* This compound was prepared according to GP3 using allylic acetate **17g** (15 mg, 0.04 mmol). After 48 h, pure *cis*-tetrahydropyran **18g** was isolated (8 mg, 64%) as a colorless oil. R_f = 0.41 (PE/EtOAc = 3:1); IR (neat) 1731, 1600, 1564, 1494, 1446, 1410, 1348, 1299, 1240, 1196, 1124, 1077, 1032, 966 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.36 (m, 3H), 7.29 (ddd, J = 8.4, 6.4, and 1.2 Hz, 2H), 7.21 (tt, J = 7.2 and 1.6 Hz, 1H), 6.60 (dd, J = 16.0 and 0.8 Hz, 1H), 6.24 (dd, J = 16.4 and 6.0 Hz, 1H), 4.46 (dd, J = 11.2 and 2.0 Hz, 1H), 4.17 (ddt_{app}, J = 10.8, 5.6, and 1.6 Hz, 1H), 3.82 (s, 3H), 1.99 (m, 1H), 1.90 (m, 1H), 1.82−1.69 (m, 2H), 1.56−1.47 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 137.1, 136.6, 130.7, 130.3, 129.9, 128.6 (2C), 127.6, 126.6 (2C), 121.1, 78.9, 72.0, 39.6, 32.3, 31.6, 23.9; LRMS (EI) m/z (rel intensity) 302 ($[M]^{\cdot+}$, 10), 267 ($[M - Cl]^+$, 13), 144 ($[3\text{-chloro-1-methylpyrazoleC}_2H_3]^{\cdot+}$, 30), 143 (18), 142 ($[3\text{-chloro-1-methylpyrazoleC}_2H_3]^{\cdot+}$, 100), 135 (27), 131 (16), 130 ($[PhC_4H_5]^{\cdot+}$, 35), 129 (39), 128 (19), 115 ($[3\text{-chloro-1-methylpyrazole-H}]^+$, 25), 91 (20), 77 ($[C_6H_5]^+$, 17); HRMS (ESI) calcd for $C_{17}H_{20}ClN_2O$ $[M + H]^+$ 303.1259, found 303.1261.

*(E)-1-(3-(6-Styryltetrahydro-2H-pyran-2-yl)-1H-indol-1-yl)-ethanone (**18h**).* This compound was prepared according to GP3 using allylic acetate **17h** (40 mg, 0.10 mmol). After 2 h, pure *cis*-tetrahydropyran **18h** was isolated (19 mg, 56%) as a pale yellow oil. R_f = 0.29 (PE/CH_2Cl_2 = 1:4); IR (neat) 1703, 1607, 1450, 1382, 1330, 1298, 1243, 1219, 1194, 1074, 1033, 966 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.44 (bd, J = 8.0 Hz, 1H), 7.67 (ddd, J = 7.6, 1.2, and 0.8 Hz, 1H), 7.41−7.38 (m, 3H), 7.36 (ddd, J = 8.4, 7.2, and 1.2 Hz, 1H), 7.33−7.26 (m, 3H), 7.23 (tt, J = 7.2 and 1.2 Hz, 1H), 6.65 (dd, J = 16.0 and 1.2 Hz, 1H), 6.32 (dd, J = 16.0 and 6.0 Hz, 1H), 4.80 (bdd, J = 10.8 and 1.6 Hz, 1H), 4.29 (ddt_{app}, J = 10.8, 5.6, and 1.6 Hz, 1H), 2.63 (s, 3H), 2.11−2.01 (m, 2H), 1.91−1.72 (m, 3H), 1.61 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.8, 137.0, 136.3, 130.7, 130.2, 128.9, 128.6 (2C), 127.7, 126.6 (2C), 125.4, 124.8, 123.6, 121.7, 119.9, 116.9, 79.0, 73.8, 31.94, 31.90, 24.2, 23.9; LRMS (EI) m/z (rel intensity) 345 ($[M]^{\cdot+}$, 17), 274 (17), 168 (17), 167 (16), 156 (19), 144 (22), 143 (66), 131 (16), 130 ($[PhC_4H_5]^{\cdot+}$, 100), 129 (36), 128 (23), 117 (19), 115 ($[indole - H]^+$, 46), 91 (21), 77 ($[C_6H_5]^+$, 19); HRMS (ESI) calcd for $C_{23}H_{24}NO_2$ $[M + H]^+$ 346.1802, found 346.1803.

*(E)-2-(6-Styryltetrahydro-2H-pyran-2-yl)-1-tosyl-1H-pyrrole (**18i**).* This compound was prepared according to GP3 using allylic acetate **17i** (50 mg, 0.11 mmol). After 45 min, pure *cis*-tetrahydropyran **18i** was isolated (5 mg, 11%) as a colorless oil. R_f = 0.50 (PE/Et_2O = 5:1); IR (neat) 1597, 1450, 1370, 1307, 1244, 1170, 1153, 1087, 1062, 1025, 1004, 980 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.71 (dt_{app}, J = 8.4 and 2.0 Hz, 2H), 7.34 (dd, J = 3.6 and 1.6 Hz, 1H), 7.32−7.29 (m, 4H), 7.24 (m, 1H), 7.01 (bdd, J = 8.4 and 0.8 Hz, 2H), 6.42 (dd, J = 16.4 and 1.6 Hz, 1H), 6.35 (ddd, J = 3.6, 1.6, and 0.8 Hz, 1H), 6.24 (td_{app}, J = 3.2 and 0.4 Hz, 1H), 5.96 (dd, J = 16.0 and 6.8 Hz, 1H), 5.02 (bdd, J = 10.4 and 2.0 Hz, 1H), 4.19 (dddd, J = 11.2, 6.8, 2.0, and 0.8 Hz, 1H), 2.11 (s, 3H), 2.00 (m, 1H), 1.89 (m, 1H), 1.85−1.68 (m, 3H), 1.43 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 144.4, 137.0, 136.7, 135.6, 130.8, 130.2, 129.7 (2C), 128.7 (2C), 127.7, 127.3 (2C), 126.5 (2C), 124.0, 113.0, 111.1, 79.0, 70.7, 31.8, 29.4, 24.0, 21.5; LRMS (EI) m/z (rel intensity) 252 ($[M - pTolSO_2]^+$, 11), 130 ($[PhC_4H_5]^{\cdot+}$, 57), 129 (11), 91 ($[pTol]^+$, 100), 65 ($[pyrrole - H]^{\cdot+}$, 12); HRMS (ESI) calcd for $C_{24}H_{25}NO_3SNa$ $[M + Na]^+$ 430.1447, found 430.1448.

*(E)-4-Chloro-7-(phenylsulfonyl)-5-(2-(6-phenyltetrahydro-2H-pyran-2-yl)vinyl)-7H-pyrrolo[2,3-d] Pyrimidine (**18j**).* This compound was prepared according to GP3 using allylic acetate **17j** (39 mg, 0.07 mmol). After 4 days, pure *cis*-tetrahydropyran **18j** was isolated (25 mg, 72%) as a yellow oil. R_f = 0.43 (PE/EtOAc = 4:1); IR (neat) 1579, 1537, 1450, 1433, 1387, 1216, 1189, 1176, 1158, 1092, 1015, 964

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cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.73 (s, 1H), 8.19 (dd, J = 8.4 and 1.2 Hz, 2H), 7.86 (d, J = 1.2 Hz, 1H), 7.64 (tt, J = 7.6 and 1.2 Hz, 1H), 7.56−7.51 (m, 2H), 7.42−7.39 (m, 2H), 7.37−7.32 (m, 2H), 7.26 (tt, J = 7.6 and 1.6 Hz, 1H), 7.07 (ddd, J = 16.0, 1.6, and 1.2 Hz, 1H), 6.31 (dd, J = 16.0 and 5.6 Hz, 1H), 4.50 (dd, J = 11.2 and 2.4 Hz, 1H), 4.24 (ddt_{app}, J = 11.2, 5.6, and 1.6 Hz, 1H), 2.04 (m, 1H), 1.92−1.74 (m, 3H), 1.63−1.50 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 153.3, 152.5, 151.6, 143.2, 137.4, 135.0, 134.6, 129.5 (2C), 128.5 (2C), 128.4 (2C), 127.5, 126.0 (2C), 122.5, 118.6, 117.8, 117.2, 80.0, 78.2, 33.7, 31.6, 24.1. LRMS (EI) m/z (rel intensity) not detected by GC-MS; HRMS (ESI) calcd for $C_{25}H_{23}ClN_3O_3S$ $[M + H]^+$ 480.1143, found 480.1143

*4-Hydroxy-4-phenylbutan-2-one (**S6**).* To an ice-cold stirred solution of benzaldehyde (667 μL, 6.60 mmol, 1.0 equiv) in acetone (9.7 mL) and H_2O (9.5 mL) was added pyrrolidine (163 μL, 1.98 mmol, 0.3 equiv), and the mixture was stirred at rt for 10 min. The solution was diluted with H_2O (60 mL) and CH_2Cl_2 (60 mL); the phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a yellow oil, which was purified by column chromatography (PE/EtOAc = 2:1) to furnish pure alcohol **S6** (656 mg, 61%) as a colorless oil. These data are in full accordance with those reported in the literature.[37] R_f = 0.35 (PE/EtOAc = 2:1); IR (neat) 3411, 1704, 1604, 1494, 1453, 1359, 1162, 1086, 1060, 1027 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36−7.25 (m, 5H), 5.15 (dt_{app}, J = 9.1 and 3.3 Hz, 1H), 3.35 (d, J = 3.2 Hz, 1H), 2.89 (ddd, J = 17.6, 8.8, and 0.4 Hz, 1H), 2.80 (ddd, J = 17.6, 3.6, and 0.4 Hz, 1H), 2.19 (bs, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 209.2, 142.8, 128.6 (2C), 127.8, 125.7 (2C), 69.9, 52.1, 30.9; LRMS (EI) m/z (rel intensity) 164 ($[M]^{\cdot+}$, 17), 146 ($[M - H_2O]^{\cdot+}$, 36), 145 (19), 131 (26), 107 ($[PhCHOH]^+$, 65), 106 (62), 105 ($[PhCO]^+$, 64), 103 (32), 79 (95), 78 (27), 77 ($[C_6H_5]^+$, 100), 58 (34), 51 (50), 50 (21).

*4-((tert-Butyldimethylsilyl)oxy)-4-phenylbutan-2-one (**S7**).* To an ice-cold stirred solution of alcohol **S6** (3.10 g, 18.88 mmol, 1.0 equiv) and imidazole (4.76 g, 69.85 mmol, 3.7 equiv) in CH_2Cl_2 (124 mL) was added TBSCl (5.12 g, 33.98 mmol, 1.8 equiv), and the mixture was stirred at rt for 18 h. A saturated aqueous solution of NH_4Cl (50 mL) and H_2O (50 mL) were added; the phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 80 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a yellow oil, which was purified by column chromatography (PE/Et_2O = 10:1) to furnish pure silyl ether **S7** (5.03 g, 96%) as a colorless oil. These data are in full accordance with those reported in the literature.[38] R_f = 0.26 (PE/Et_2O = 8:1); IR (neat) 1719, 1494, 1472, 1360, 1253, 1162, 1088, 1004 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35−7.22 (m, 5H), 5.15 (dd, J = 8.8 and 4.0 Hz, 1H), 2.94 (dd, J = 14.8 and 8.8 Hz, 1H), 2.54 (dd, J = 14.8 and 4.0 Hz, 1H), 2.15 (s, 3H), 0.84 (s, 9H), 0.01 (s, 3H), −0.18 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 207.4, 144.6, 128.4 (2C), 127.5, 125.9 (2C), 72.1, 54.5, 32.0, 25.9 (3C), 18.2, −4.6, −5.1; LRMS (EI) m/z (rel intensity) 221 ($[PhCHOTBS]^+$, 31), 117 (16), 116 (11), 115 ($[Me_2tBuSi]^+$, 100), 75 ($Me_2SiOH]^+$, 41), 73 (13).

*(E)-1-((tert-Butyldimethylsilyl)oxy)-5-hydroxy-1,7-diphenylhept-6-en-3-one (**S8**).* To an ice-cold stirred solution of diisopropylamine (1.71 mL, 12.07 mmol, 1.2 equiv) in dry THF (70 mL) under argon was added dropwise *n*-BuLi (2.5 M in hexanes, 4.83 mL, 12.07 mmol, 1.2 equiv), and the mixture was stirred at 0 °C for 15 min. The reaction was then cooled to −78 °C, and a solution of methyl ketone **S7** (2.80 g, 10.06 mmol, 1.0 equiv) in dry THF (12 mL) was added dropwise. The resulting mixture was stirred at −78 °C for 1.5 h, and cinnamaldehyde (1.52 mL, 12.07 mmol, 1.2 equiv) was added slowly. The solution was stirred at −78 °C, and after 2 h, a saturated aqueous solution of NH_4Cl (25 mL) and H_2O (25 mL) were added; the phases were separated, and the aqueous layer was extracted with Et_2O (2 × 60 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a yellow liquid, which was purified by column chromatography (PE/Et_2O = 4:1) to furnish pure alcohol **S8** (1.41 g, 34%) as a colorless oil as a 60:40 mixture of diastereomers. R_f = 0.19 (PE/CH_2Cl_2 = 1:2); IR (neat) 3435, 1710, 1494, 1471, 1361, 1253, 1068, 1004, 966 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.22 (m, 10H), 6.63 (dd, J = 15.6 and 1.2 Hz, 0.4H), 6.62 (dd, J = 16.4 and 1.2 Hz, 0.6H), 6.19 (dd, J = 16.0 and 6.0 Hz, 0.4H), 6.18 (dd, J = 16.0 and 6.0 Hz, 0.6H), 5.20 (m, 1H), 4.77 (m, 0.4H), 4.72 (m, 0.6H), 3.23 (d, J = 3.6 Hz, 0.6H), 3.21 (d, J = 3.7 Hz, 0.4H), 2.99 (dd, J = 15.2 and 8.8 Hz, 0.6H), 2.98 (dd, J = 14.8 and 9.2 Hz, 0.4H), 2.86−2.55 (m, 3H), 0.86 (s, 9H), 0.04 (s, 1.8H), 0.03 (s, 1.2H), −0.16 (s, 1.8H), −0.17 (s, 1.2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ [209.64 and 209.55], [144.20 and 144.18], 136.7, 130.4, [130.22 and 130.19], 128.7 (2C), 128.5 (2C), 127.8, 127.7, 126.6 (2C), [125.9 (2C) and 125.8 (2C)], [72.0 and 71.8], [68.5 and 68.3], [54.5 and 54.3], [51.3 and 51.1], [25.88 (3C) and 25.87 (3C)], 18.2, [−4.58 and −4.59], [−5.0 and −5.1]; LRMS (EI) m/z (rel intensity) 221 ($[PhCHOTBS]^+$, 36), 117 (14), 116 (11), 115 ($[Me_2tBuSi]^+$, 100), 103 (10), 77 ($[C_6H_5]^+$, 10), 75 ($[Me_2SiOH]^+$, 59), 73 (16); HRMS (ESI) calcd for $C_{25}H_{34}O_3SiNa$ $[M + Na]^+$ 433.2169, found 433.2168.

*(E)-1,5-Dihydroxy-1,7-diphenylhept-6-en-3-one (**13**).* To an ice-cold stirred solution of silyl ether **S8** (72 mg, 0.18 mmol, 1.0 equiv) in dry THF (3 mL) under argon were added AcOH (101 μL, 1.75 mmol, 10.0 equiv) and TBAF (1 M in THF, 877 μL, 0.88 mmol, 5.0 equiv), and the mixture was stirred at 50 °C for 48 h. A saturated aqueous solution of Na_2CO_3 (10 mL) and EtOAc (5 mL) were added; the phases were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a yellowish oil, which was purified by column chromatography (pentane/EtOAc = 1:1) to furnish diol **13** (37 mg, 71%) as a colorless oil as a 60:40 mixture of diastereomers. R_f = 0.43 (PE/EtOAc = 1:1); IR (neat) 3391, 1704, 1600, 1494, 1450, 1385, 1200, 1059, 967 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.23 (m, 10H), 6.63 (bd, J = 16.0 Hz, 1H), 6.19 (dd, J = 16.0 and 6.2 Hz, 1H), 5.20 (m, 1H), 4.79 (m, 1H), 3.33 (bs, 1H), 3.16 (bs, 1H), 2.96 (m, 1H), 2.85−2.69 (m, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ [210.7 and 210.6], [142.81 and 142.77], 136.5, 130.7, [130.2 and 130.1], 128.7 (4C), 127.94, 127.92, 126.6 (2C), [125.75 (2C) and 125.72 (2C)], [70.2 and 70.0], [68.8 and 68.6], [52.4 and 52.3], [50.4 and 50.3]; LRMS (EI) m/z (rel intensity) 132 (61), 131 ([cinnamaldehyde]$^{\cdot+}$, 100), 104 ($[PhC_2H_3]^{\cdot+}$, 23), 103 ($[PhC_2H_2]^{\cdot+}$, 53), 78 (31), 77 ($[C_6H_5]^+$, 41), 51 (36); HRMS (ESI) calcd for $C_{19}H_{20}O_3Na$ $[M + Na]^+$ 319.1305, found 319.1299.

*2-Phenyl-6-((E)-styryl)dihydro-2H-pyran-4(3H)-one (**14**).* To a stirred solution of diol **13** (90 mg, 0.30 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL) was added powdered $FeCl_3{\cdot}6H_2O$ (4.1 mg, 0.015 mmol, 0.05 equiv), and the mixture was stirred at rt for 30 h. The solvent was removed under reduced pressure to give an orange oil, which was purified by column chromatography (pentane/CH_2Cl_2 = 1:4) to yield *cis*-tetrahydropyranone **14** (52 mg, 62%) as a colorless oil. R_f = 0.40 (PE/CH_2Cl_2 = 1:4); IR (neat) 1717, 1600, 1496, 1450, 1335, 1308, 1241, 1148, 1052, 965 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45−7.38 (m, 6H), 7.36−7.31 (m, 3H), 7.26 (tt_{app}, J = 7.6 and 1.6 Hz, 1H), 6.70 (d, J = 16.4 Hz, 1H), 6.33 (dd, J = 16.0 and 6.0 Hz, 1H), 4.77 (dd, J = 9.4 and 5.1 Hz, 1H), 4.49 (m, 1H), 2.71−2.57 (m, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 206.2, 140.7, 136.3, 131.7, 128.8 (2C), 128.7 (2C), 128.3, 128.2 (2C), 126.8 (2C), 125.9 (2C), 79.0, 77.8, 49.7, 47.9; LRMS (EI) m/z (rel intensity) 278 ($[M]^{\cdot+}$, 1), 260 ($[M - H_2O]^{\cdot+}$, 1), 131 (18), 130 ($[PhC_4H_5]^{\cdot+}$, 11), 129 (14), 105 (21), 104 ($[PhC_2H_3]^{\cdot+}$, 100), 103 (14), 78 (15), 77 ($[C_6H_5]^+$, 18); HRMS (ESI) calcd for $C_{19}H_{18}O_2Na$ $[M + Na]^+$ 301.1199, found 301.1198.

*6-(2-Chloropyridin-3-yl)tetrahydro-2H-pyran-2-carbaldehyde (**21**).* To a stirred solution of alkene **18b** (85 mg, 0.28 mmol, 1.0 equiv) and NMO (50 mg, 0.43 mmol, 1.5 equiv) in H_2O/*t*BuOH (1:1, 6 mL) under argon was slowly added a solution of OsO_4 (0.079 M in *t*BuOH, 72 μL, 0.006 mmol, 0.02 equiv), and the mixture was stirred at rt for 3 h. The reaction was quenched with an aqueous solution of $Na_2S_2O_3$ (5 mL), and EtOAc (8 mL) was added. The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The organic layers were combined, dried over $MgSO_4$, and

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filtered, and the solvents were removed under reduced pressure to give a beige solid, which was purified by column chromatography (PE/EtOAc = 1:3) to furnish diol **20** (80 mg, 84%) as a white sticky foam. To a stirred solution of diol **20** (50 mg, 0.15 mmol, 1.0 equiv) in THF/buffer pH 7 (1/1, 3 mL) was added $NaIO_4$ (96 mg, 0.45 mmol, 3 equiv). The mixture was stirred at rt for 3 h before adding EtOAc (5 mL) and H_2O (5 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 5 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give a yellow oil, which was purified by column chromatography (pentane/acetone = 3:1) to furnish pure aldehyde **21** (31 mg, 92%) as a colorless oil. R_f = 0.51 (PE/acetone = 3:1); IR (neat) 2858, 1736, 1583, 1564, 1439, 1413, 1361, 1300, 1266, 1188, 1087, 1039 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.70 (s, 1H), 8.31 (dd, J = 4.4 and 2.0 Hz, 1H), 7.97 (ddd, J = 7.6, 2.0, and 0.4 Hz, 1H), 7.29 (ddd, J = 8.0, 4.8, and 0.4 Hz, 1H), 4.77 (dd, J = 10.8 and 2.0 Hz, 1H), 4.05 (dd, J = 12.0 and 2.8 Hz, 1H), 2.13 (m, 1H), 2.06 ($dquint_{app}$, J = 13.6 and 3.2 Hz, 1H), 1.96 (m, 1H), 1.80 (qt_{app}, J = 13.2 and 3.6 Hz, 1H), 1.46 (qd_{app}, J = 12.8 and 4.4 Hz, 1H), 1.31 (tdd_{app}, J = 13.2, 10.8, and 3.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 201.1, 148.5, 148.4, 136.8, 136.3, 123.1, 82.2, 76.2, 31.8, 25.9, 23.1; LRMS (EI) m/z (rel intensity) 198 ($[M - CHO]^+$, 35), 196 ($[M - CHO]^+$, 100), 152 (23), 126 (34), 117 (22), 116 (20), 104 (15), 77 (20), 55 (28), 51 (22); HRMS (ESI) calcd for $C_{11}H_{13}ClNO_2$ $[M + H]^+$ 226.0629, found 226.0630.

*(6-(2-Chloropyridin-3-yl)tetrahydro-2H-pyran-2-yl)methanol (**22**).* To an ice-cold stirred solution of aldehyde **21** (25 mg, 0.11 mmol, 1.0 equiv) in EtOH (3 mL) was added $NaBH_4$ (8.4 mg, 0.22 mmol, 2.0 equiv), and the mixture was stirred at rt for 4 h. The solution was evaporated under reduced pressure, and the residue was taken up in CH_2Cl_2 (4 mL) and H_2O (4 mL). The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 4 mL). The organic layers were combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure to give alcohol **22** (24 mg, 95%) as a colorless oil. R_f = 0.38 (PE/acetone = 3:1); IR (neat) 3373, 1566, 1413, 1375, 1187, 1088, 1046 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.28 (dd, J = 4.8 and 2.0 Hz, 1H), 7.87 (ddd, J = 7.6, 2.0, and 0.4 Hz, 1H), 7.25 (ddd, J = 7.6, 4.8, and 0.4 Hz, 1H), 4.70 (dd, J = 11.2 and 2.4 Hz, 1H), 3.71 (m, 1H), 3.67−3.59 (m, 2H), 2.23 (bs, 1H, OH), 2.06 (m 1H), 1.97 (m, 1H), 1.75 (qt_{app}, J = 13.2 and 4.0 Hz, 1H), 1.60 (m, 1H), 1.36 (tdd_{app}, J = 12.8, 10.8, and 4.0 Hz, 1H), 1.26 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 148.6, 148.2, 137.5, 136.3, 123.0, 79.1, 76.0, 66.4, 32.1, 26.9, 23.3; LRMS (EI) m/z (rel intensity) 211 ($[M - H_2O]^{\cdot+}$, 3), 209 ($[M - H_2O]^{\cdot+}$, 13), 198 ($[M - CH_2OH]^+$, 32), 196 ($[M - CH_2OH]^+$, 100), 142 (34), 126 (19), 106 (20), 104 (15), 78 (17), 77 (15), 57 (31), 51 (17); HRMS (ESI) calcd for $C_{11}H_{15}ClNO_2$ $[M + H]^+$ 228.0786, found 228.0785.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra for substrates and products. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02371.

^1H and ^{13}C NMR spectra for substrates and products of **S1**, **S2**, **S3**, **3**, **5**, **6**, **9**, **10**, **11**, **15d−15i**, and **16b−16j** (PDF)

^1H and ^{13}C NMR spectra for substrates and products of **S6**, **S7**, **S8**, **4**, **7a−7c**, **8**, **12a−12b**, **13**, **14**, **17b−17j**, **18b−18j**, **21**, and **22** (PDF)

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Notes

The authors declare no competing financial interest.

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(23) The reaction was tested in boiling deionized water in the absence of any catalyst according to ref 7; after 3 h, full conversion of **17b** was observed, but a low diastereomeric ratio was obtained (*cis*/*trans* = 62:38) even after 48 h.
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