Organic &
Biomolecular Chemistry

ROYAL SOCIETY
OF CHEMISTRY

PAPER

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Cite this: *Org. Biomol. Chem.*, 2025, **23**, 10701

Diastereoselective intramolecular oxidopyrylium–alkene [5 + 2]-cycloaddition of substrates with a β-chiral center on alkene tethers: synthesis of 8-oxabicyclo-[3.2.1]-octenone heterocycles

Arun K. Ghosh *[a,b] and Denver Hopkins[a]

Received 4th September 2025,
Accepted 27th October 2025

DOI: 10.1039/d5ob01429h

rsc.li/obc

We investigated the asymmetric intramolecular oxidopyrylium–alkene [5 + 2]-cycloaddition reaction of substrates bearing tethered alkenes containing β-chiral centers. The effect on the cycloadduct diastereoselectivity was examined for carbon chain tethered alkenes or alkoxy tethered alkenes with varying chain lengths that can form 5-, 6- and 7-membered rings. We also probed the effect of varying steric bulk on the β-chiral center substituents on cycloadduct diastereoselectivity. Various substrates with carbon chain tethered alkenes were synthesized using the Lewis acid mediated conjugate addition of an allyl group to furanyl enones. Reduction of the resulting ketones followed by the Achmatowicz reaction of furanyl alcohol provided oxidopyrylium–alkene substrates. The asymmetric [5 + 2]-cycloaddition proceeded with high diastereoselectivity for cycloadducts with five and six-membered rings. However, cycloadducts with a seven-membered ring showed no diastereoselectivity. Stereochemical models are provided to explain the high diastereoselectivity for five and six-membered products.

Introduction

The oxidopyrylium–alkene [5 + 2]-cycloaddition provides convenient access to functionalized 8-oxabicyclo-[3.2.1]-octenone heterocycles with multiple stereogenic centers.[1,2] Over the years, the gradual development of these cycloaddition reactions led to their practical applications in organic synthesis.[3,4] In particular, these seven-membered ring systems containing an oxygen bridge have been utilized in the synthesis of natural products.[5,6] These intramolecular oxidopyrylium–alkene [5 + 2]-cycloadditions are especially attractive as the resulting cycloadducts conveniently generate a highly functionalized oxabridged bicyclic framework for a variety of synthetic and medicinal chemistry applications.[7–9] Despite their potential uses, the development of asymmetric intramolecular oxidopyrylium–alkene cycloaddition is relatively underexplored.[2,7,10] The early examples of asymmetric intramolecular cycloaddition reactions with chiral centers on the tether include the synthesis of (+)-phorbol by Wender and co-workers, as shown in Fig. 1.[11,12] Asymmetric [5 + 2]-cycloaddition of acetate derivative **1** containing α- and β-chiral centers on the side chain alkene tether was carried out to provide cycloadduct **2** as a single diastereomer in excellent yield.[11,12] The cycloadduct was later converted to (+)-phorbol, which is a tumor promoting agent that activates protein kinase C.[13] Mascareñas and co-workers examined asymmetric induction of alkenesulfinyl substrate **3** to provide the product cycloadduct **4** with high diastereoselectivity (dr 97 : 3) and excellent yield.[14,15] Trivedi and co-workers reported an asymmetric [5 + 2]-cycloaddition of isopropylidene derivative **5** containing α, β, and γ-chiral centers on the side chain tether.[16] This reaction proceeded with excellent diastereoselectivity (dr 97 : 3) and good yield, affording cycloadduct **6**. Subsequently, other intermolecular and intramolecular asymmetric oxidopyrylium–alkene cycloaddition reactions have been reported.[17–23] We recently investigated the intramolecular asymmetric oxidopyrylium–alkene [5 + 2]-cycloaddition of substrates that contain an α-alkoxy chiral center **7**, which provided cycloadduct **8** with high diastereoselectivity and isolated yield.[24] In a systematic study, we investigated the effect of the size of alkyl groups on the α-chiral center and the alkoxy alkene tether length on diastereoselectivity.[24] We now investigate the ability of substrates **9** with alkene tethers and alkoxy alkene tethers containing a β-chiral center to direct [5 + 2]-cycloaddition reactions to provide **10**. The effect on the cycloadduct diastereoselectivity was examined for varying chain lengths that can form 5-, 6-, and 7-membered rings. We also examined the effect of steric bulk on the β-chiral center substituents on cycloadduct diastereoselectivity.

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[a] *Department of Chemistry, Purdue University, 560 Oval Drive, West Lafayette, IN 47907, USA. E-mail: akghosh@purdue.edu; Tel: +1 765 4945323*
[b] *Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University, 560 Oval Drive, West Lafayette, IN 47907, USA*

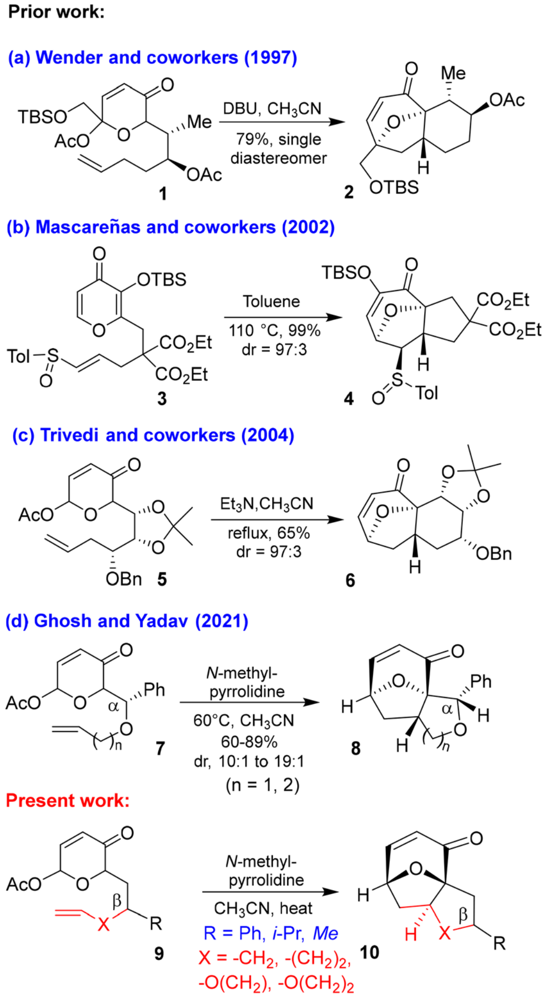
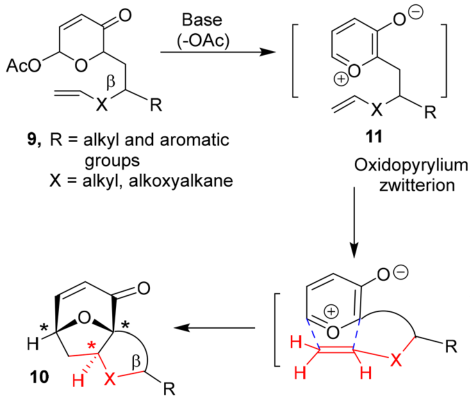


Fig. 1 Prior works on asymmetric intramolecular oxidopyrylium–alkene [5 + 2]-cycloaddition of substrates.

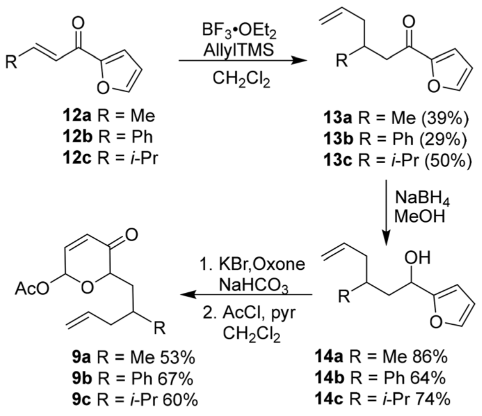
Results and discussion

In this work, we investigate intramolecular oxidopyrylium–alkene [5 + 2]-cycloaddition of substrates containing a β-alkyl or aryl substituted alkene tether that would form new five to seven membered exocyclic rings on 8-oxabicyclo-[3.2.1]-octenone heterocycles, as shown in Scheme 1. Upon exposure to a base, substrates **9** leads to oxidopyrylium ylide **11,** which undergoes [5 + 2]-cycloaddition to provide cycloadduct **10**. We postulate that the cycloaddition proceeds diastereoselectively through transition state **11,** wherein the bulky alkyl or aryl substituent will occupy a pseudo-equatorial or equatorial position depending upon the ring size to avoid developing non-bonded interactions. We expect that the stereochemical outcome will be influenced by the size of the alkyl or aryl substituents as well. We planned to investigate the cycloadduct diastereoselectivity associated with substrates containing varying tether lengths and substituent sizes.

Our synthesis of various substrates containing the β-substituent leading to the formation of a 5-membered exocyclic cyclopentane ring is shown in Scheme 2. Our synthetic plan was to carry out conjugate addition to elongate the allyl chain using readily available enones **12**. However, initial attempts under Gilman conditions with enone **12a** were unsuccessful, providing only trace amounts of the conjugate addition product **13a**, as shown in Table 1 (entries 1–3).[25,26] The reaction of **13a** with allyl magnesium bromide in the presence of the CuBr.DMS complex in THF at −78 °C to 0 °C resulted in tertiary alcohol **15** with 68% yield (entry 3). We attempted the traditional Sakurai–Hosomi reaction[27,28] using allyltrimethylsilane in the presence of $TiCl_4$, which resulted in the desired product **13a** with 8% yield (entry 4). Other Lewis acids such as $InCl_3$, $Sc(OTf)_3$, or $Bi(OTf)_3$ did not lead to any improvement in the yield (entries 5–7). However, the reaction of **12a** with allyltrimethylsilane in the presence of $BF_3{\cdot}OEt_2$ resulted in a conjugate addition product **13a** in 39% yield (entry 8). A significant amount of the unreacted starting material was recovered (61% recovery of the starting material). These conditions were then used for reactions with other enones. The reaction of enone **12b** with allyltrimethylsilane and $BF_3{\cdot}OEt_2$ provided addition product **13b** in 29% yield.

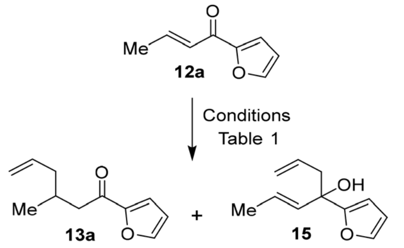


Scheme 1 Basic strategy for [5 + 2]-cycloadditions with alkene and alkoxy alkene tethers containing a β-chiral center.



Scheme 2 Syntheses of substrates **9a–c** containing all carbon alkene tethers.

Table 1 Optimization of 1,4-addition reactions

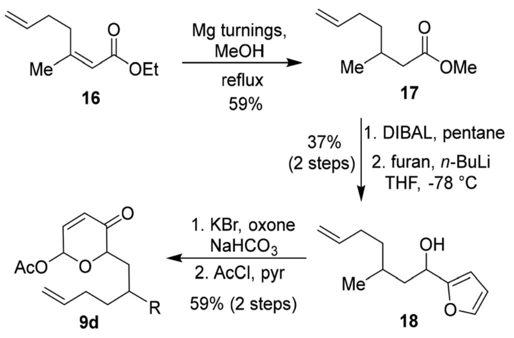


Entry	Conditions	Yield **13a** (%)	Yield **15** (%)
1	AllylBr, *n*-BuLi, CuCN, THF, −78 °C to 0 °C	Trace	Trace
2	AllylBr, *n*-BuLi, CuCN·LiCl, THF, −78 °C to 0 °C	np	np
3	AllylMgBr, CuBr·DMS, THF, −78 °C to 0 °C[a]	<5	68
4	AllylTMS, $TiCl_4$, CH_2Cl_2, −78 °C	8	0
5	$InCl_3$, TMSCl, AllylTMS, CH_2Cl_2, 23 °C	np	np
6	$Sc(OTf)_3$, AllylTMS, CH_2Cl_2, 0 °C to 23 °C	np	np
7	$Bi(OTf)_3$, AllylTMS, CH_2Cl_2, 0 °C to 23 °C	np	np
8	BF_3·OEt_2, AllylTMS, CH_2Cl_2, −78 °C to 10 °C	39[b]	0

[a] 10–30 min reactions. [b] 61% recovery of the starting material. np: no product.

Similarly, the reaction of enone **12c** provided addition product **13c** in 50% isolated yield. Reduction of ketones **13a–c** with $NaBH_4$ in MeOH at 23 °C for 2.5 h furnished furyl alcohols **14a–c** as a mixture of diastereomers in very good yields. Achmatowicz reactions[29,30] of these alcohols using Oxone in the presence of KBr and $NaHCO_3$ in aqueous THF (4 : 1) at 0 °C furnished the corresponding lactols, which were reacted with acetyl chloride in the presence of pyridine at 0 °C for 20–30 min to provide acetoxypyranone derivatives **9a–c** in good yields over 2 steps (53–67%).

The synthesis of the β-substituted carbon tethered substrate leading to the formation of a 6-membered ring is shown in Scheme 3. The known diene **16** was prepared using the Horner–Wadsworth–Emmons reaction, as described in the literature.[31] Exposure of diene **16** to elemental magnesium in MeOH at 65 °C for 4 h resulted in selective 1,4-reduction and ester exchange, providing methyl ester **17** in 59% yield.[32]

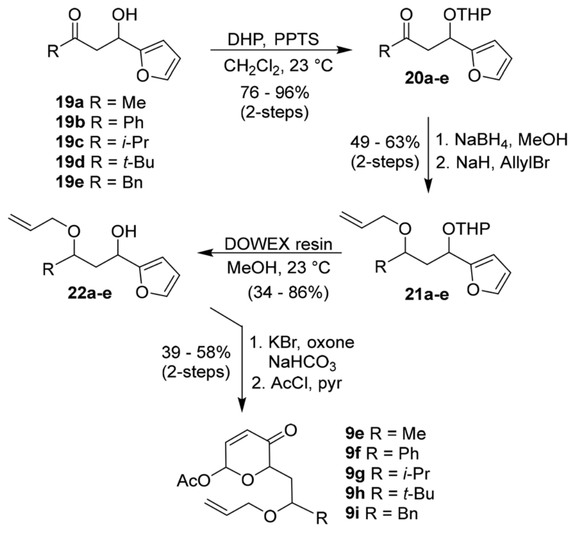


Scheme 3 Synthesis of substrate **9d** with carbon tethers.

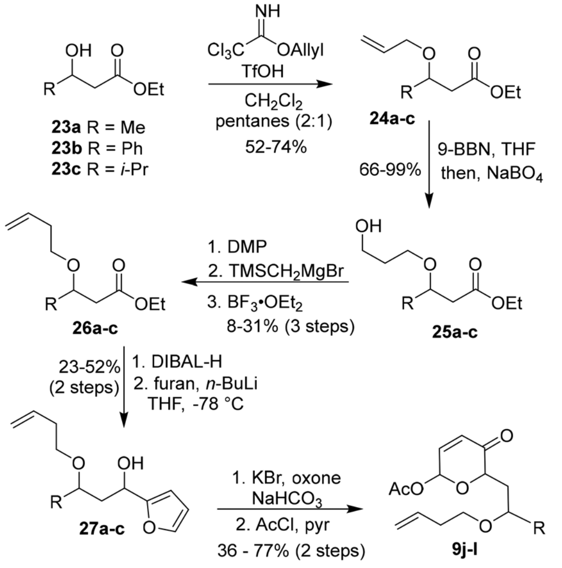
DIBAL-H reduction of **17** at −78 °C in *n*-pentane for 30 min provided a crude aldehyde. The reaction of the resulting aldehyde with 2-lithiofuran at −78 °C in THF for 30 min provided furanol **18** in 37% yield over 2 steps. Achmatowicz reactions of furanol **18** gave a lactol, which upon reaction with acetyl chloride in the presence of pyridine provided acetoxypyranone **9d** in 59% yield over 2 steps.

The synthesis of various substrates containing alkoxy alkene tethers for the formation of a substituted tetrahydropyran ring is shown in Scheme 4. Various β-hydroxy ketone derivatives **19a–d** were prepared using an aldol reaction, as described in the literature.[33] These β-hydroxy ketone derivatives were protected as tetrahydropyran (THP) ethers using 3,4-dihydro-2*H*-pyran (DHP) and pyridinium *p*-toluenesulfonate (PPTS) in CH_2Cl_2 at 23 °C for 14–72 h to provide the respective THP ethers **20a–e** in good to excellent yields (76–96%). The ketone derivatives were reduced with $NaBH_4$ in MeOH at 23 °C with high yields. The resulting alcohols were converted to allyl ethers **21a–e** with NaH and allyl bromide in THF at 23 °C for 14–22 h in 49–63% yields over two steps. Exposure of **21a–e** to DOWEX-50W-X8 resin in MeOH at 23 °C provided the respective furanyl alcohols **22a–e** in 34–86% yields. These alcohols were converted to acetoxypyranone derivatives **9e–i** by the Achmatowicz reaction,[29,30] followed by protection of the resulting lactols as acetate derivatives in 39–58% yields over two steps.

We also planned to explore the stereochemical outcome for the formation of 7-membered exocyclic rings. The synthesis of various requisite substrates is shown in Scheme 5. Commercially available β-hydroxy esters **23a–c** were converted to allyl ethers using *O*-allyl trichloroacetimidate in the presence of a catalytic amount of triflic acid in a mixture (2 : 1) of CH_2Cl_2 and pentanes at 23 °C for 15–19 h to provide allyl ethers **24a–c** in 52–74% yields.[34,35] Hydroboration of alkenes with 9-BBN in THF at 23 °C for 1.5–2.5 h, followed by work up



Scheme 4 Synthesis of various substrates **9e–i** containing the alkoxy alkene tethers for six-membered exocyclic rings.

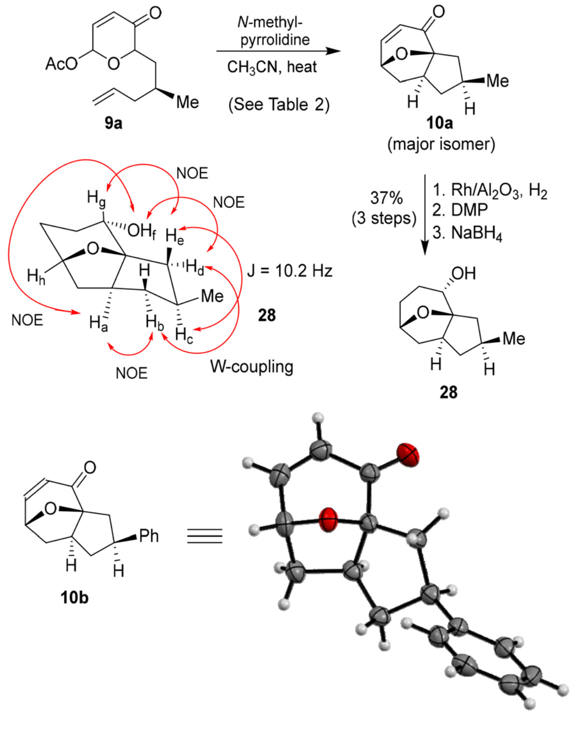


Scheme 5 Synthesis of alkoxy alkene substrates **9j–l** for 7-membered rings.

with sodium perborate tetrahydrate furnished alcohols **25a–c** in 66–99% yields. DMP oxidation of these alcohols afforded the corresponding aldehydes in excellent yields. To extend the chain length, a one-carbon Wittig reaction of the resulting aldehyde from **26a** was attempted; however, no alkene product was formed. However, the Peterson olefination provided reproducible results.[36–38] The reaction of aldehydes from **25a–c** with $TMSCH_2MgBr$ provided the corresponding addition products. The base-catalyzed elimination was not satisfactory. However, treatment with $BF_3 \cdot OEt_2$ at −78 °C for 1.5 to 3 h resulted in the respective olefins **26a–c** in 8–31% yields (3-steps). DIBAL-H reduction followed by reaction of the resulting aldehyde with 2-lithiofuran provided furanols **27a–c** in 23–52% yields over two steps. Achmatowicz reactions[29,30] followed by acetylation of the resulting lactols furnished the acetate derivatives **9j–l** in 36–77% yields.

For our investigation of [5 + 2]-cycloadditions with β-substitution, we first examined reactions in CH_3CN at low concentration in the presence of *N*-methylpyrrolidine (NMP) at 60 °C. These conditions were previously used for α-substituted substrates.[24] However, no product was formed under these reaction conditions, and the starting material was fully recovered. These reactions with β-substituted acetoxypyranones, in general, required higher temperature and a bit longer reaction time compared to substrates with α-substituted acetoxypyranones. Under the optimized reaction conditions, we carried out the reaction in a sealed tube containing the substrate (0.02 M in CH_3CN) and 1.5 equiv. of NMP at 150 °C oil bath temperature. The reaction of substrate **9a** proceeded smoothly under these specified conditions within 3 h, affording the [5 + 2]-cycloadduct **10a** as a major product along with its minor diastereomer in 95% yield. These diastereomers could not be separated by silica gel chromatography. Their diastereomeric ratio (dr) was determined to be 6.5 : 1 by using ^{1}H-NMR analysis. ^{1}H-NMR NOESY correlation studies of **10a** were difficult due to overlapping aliphatic protons. Therefore, the relative stereochemistry was determined after the conversion of enone **10a** to alcohol **28** through a three-step sequence. Catalytic hydrogenation of **10a** over the Rh/Al_2O_3 catalyst afforded a mixture of (1 : 1) alcohols, which upon DMP oxidation provided the saturated ketone. Reduction of the ketone using $NaBH_4$ in MeOH provided alcohol **28** as a major diastereomer (dr 10 : 1 by ^{1}H-NMR analysis) in 37% yield over 3 steps. The relative stereochemistry of **28** was supported by 1D and 2D NMR studies. The ring junction proton H_a exhibited a NOESY correlation to H_b. In addition, NOESY correlations were observed for H_a–H_f and H_d–H_f. A W-coupling between H_b–H_d indicated that both were pseudo-equatorial. Furthermore, H_e–H_c coupling constant analysis[39,40] revealed an *anti*-relationship, placing the methyl group in a pseudo-equatorial position (*syn*-relationship to H_e) as depicted. The relative stereochemistry of the corresponding phenyl substituted derivative **10b** was determined by single crystal X-ray studies. The ORTEP picture supports the assigned stereochemistry of **10b** (Scheme 6).[41,42]

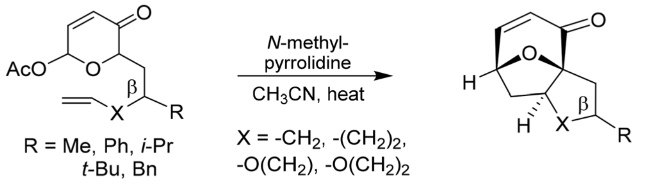
We examined the effect of the size and nature of the substituents on the stereochemical outcome. The results are shown in Table 2. The cycloaddition of substrate **9b** containing a β-phenyl substituent proceeded very well under the above-mentioned reaction conditions. The reaction of **9b** furnished [5 +



Carbon = black, oxygen = red, and hydrogen = white

Scheme 6 [5 + 2]-Cycloadditions of substrate **9a**, NOE studies of **28**, and ORTEP picture of **10b**.

Table 2 Substrate scope and diastereoselectivity of various intramolecular [5 + 2]-cycloaddition reactions



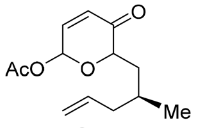
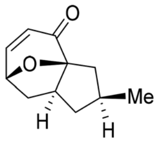
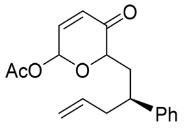
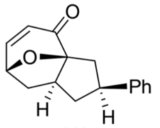
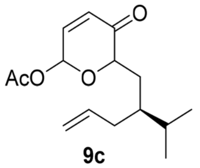
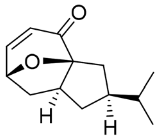
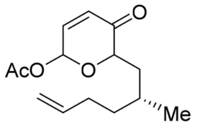
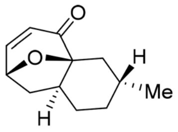
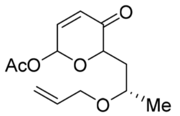
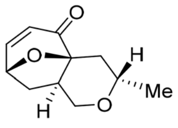
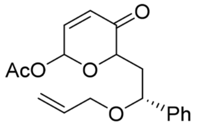
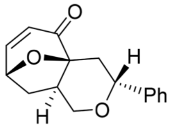
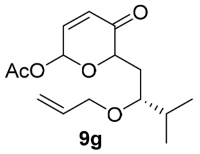
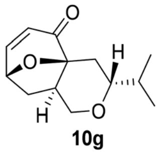
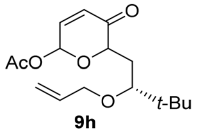
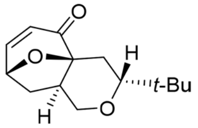
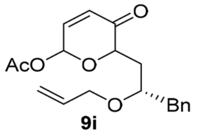
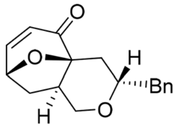
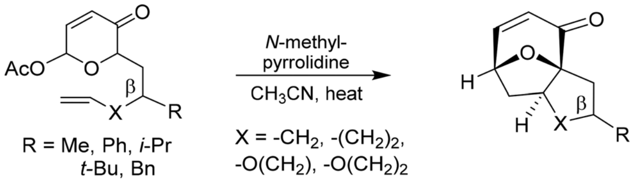
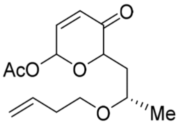
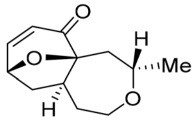
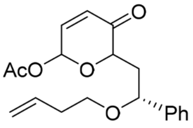
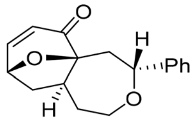
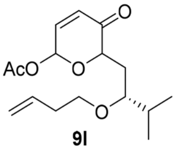
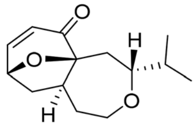
Entry	Acetoxypyranone	Cycloadduct[a]	Time (h)	Yield[b] (%)	dr[c]
1	 **9a**	 **10a**	3	95	6.5 : 1
2	 **9b**	 **10b**	4	99	12.5 : 1
3	 **9c**	 **10c**	7	99	9.5 : 1
4	 **9d**	 **10d**	3	99	3 : 1
5	 **9e**	 **10e**	8	88	9 : 1
6	 **9f**	 **10f**	3	75	6 : 1
7	 **9g**	 **10g**	7	96	9 : 1
8	 **9h**	 **10h**	5	94	9 : 1
9	 **9i**	 **10i**	4.25	59	10 : 1

Table 2 *(Contd.)*



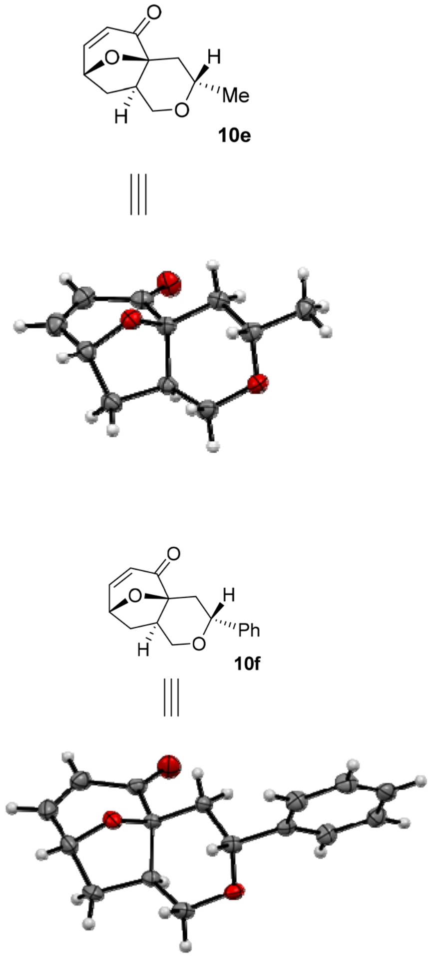
Entry	Acetoxypyranone	Cycloadduct[a]	Time (h)	Yield[b] (%)	dr[c]
10	 **9j**	 **10j**	30	67[d]	1 : 1
11	 **9k**	 **10k**	96	33[d]	1 : 1
12	 **9l**	 **10l**	80	40[d]	1 : 1

[a] Reactions were carried out using *N*-methylpyrrolidine and NMP (1.5 equiv.) in CH_3CN (0.02 M) at 150 °C. [b] Yield refers to the combined yield of both the major and minor diastereomers. [c] The diastereomeric ratios were determined by ^1H NMR. [d] Reaction was carried out at 150 °C with 4 equiv. of 2,2,6,6-tetramethylpiperidine as the base.

2]-cycloadduct **10b** as a major product along with its minor diastereomer in a nearly quantitative yield (entry 2). The presence of the phenyl group resulted in improvement of diastereoselectivity compared to the methyl group. The cycloaddition reaction with isopropyl substituted acetoxypyranone **9c** also proceeded well to provide cycloadduct **10c** as a major diastereomer with excellent yield and diastereoselectivity (entry 3). We then examined the cycloaddition of methyl substituted acetoxypyranone **9d** with a six-carbon tether length. The reaction resulted in cycloadduct **10d** as a major product along with its minor diastereomer in 99% yield (entry 4). However, the diastereoselectivity was reduced significantly (3 : 1) compared to reactions that formed five-membered exocyclic rings (entries 1–3).

We further investigated the [5 + 2]-cycloaddition of the substrate **9e** with an alkenyloxy tether containing a methyl substitution. The reaction was carried out as described above in a sealed tube and afforded cycloadduct **10e** as the major product along with its minor diastereomer in excellent yield with very good diastereoselectivity (dr 9 : 1, entry 5). However, the reaction took a bit longer to reach completion. The cycloadduct **10e** was recrystallized from chloroform. The relative stereochemistry of **10e** was determined by X-ray crystallography.[41,43] The ORTEP picture (Fig. 2) shows the relative stereochemistry of three new chiral centers that formed during the reaction. The phenyl substituted acetoxypyranone **9f** provided cycloadduct **10f** along with its minor diastereomer in 75% yield with a slight reduction in diastereoselectivity (entry 6). The relative stereochemistry of **10f** was also determined by X-ray crystallography.[41,43] The ORTEP picture is shown in Fig. 2. The isopropyl substituted substrate **9g** furnished product **10g** in excellent yield with excellent diastereoselectivity (entry 7). However, the reaction time was 7 h. The allyloxy substrate **9h** containing the *t*-butyl substitution also furnished product **10h** and its minor diastereomer with excellent yield and diastereoselectivity (entry 8). The benzyl substituted substrate **9i** provided product **10i** with excellent diastereoselectivity. However, the reaction yield was lower (59%) compared to other alkyloxy substrates (entries 5–8).

We then expanded the substrate scope to seven-membered rings. Acetoxypyranone **9j** with a β-methyl substitution was subjected to cycloaddition conditions as described above. However, the reaction provided a 1 : 1 mixture of inseparable diastereomers with a combined low yield of 22%. The reaction of **9j** with increasing equivalents of NMP did not improve the yield or diastereoselectivity. We switched the base to 2,2,6,6-tetramethylpiperidine (TMP), but with 1.5 equiv. of the base, the reaction did not provide any appreciable amount of the product.[44] However, upon increasing the equiv. of the base to 4, the cycloaddition afforded 67% yield in 30 h, but the diastereoselectivity was not improved (entry 10). When the steric bulk was increased for substrates **9k** and **9f** with isopropyl and phenyl substitution, the cycloaddition required much longer times, 96 h and 80 h, respectively. The product yields were significantly reduced and the diastereoselectivity did not improve (entries 11 and 12).



Carbon = black, oxygen = red, and hydrogen = white

Fig. 2 ORTEP pictures of major isomers **10e** and **10f**.

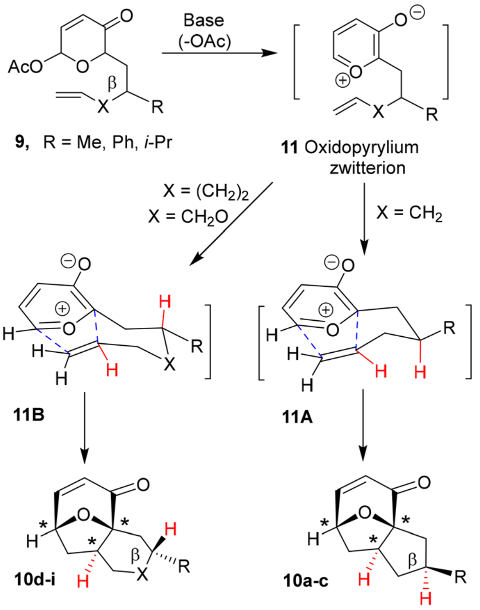


Fig. 3 Stereochemical models for [5 + 2]-cycloadditions of substrates containing β-chiral centers on the tether.

Overall, [5 + 2]-cycloaddition of substrates containing β-substitutions proceeded very well for the formation of five- and six-membered exocyclic rings. The carbon-tethered substrate **9a** with a methyl substitution showed very good diastereoselectivity for product **10a**. Increasing the steric bulk on the tether consistently improved the diastereoselectivity for products **10b** and **10c**. The carbon-tethered substrate **9d** showed excellent yield but the diastereoselectivity was reduced. On the other hand, cycloaddition of the oxygen-tethered substrates leading to 6-membered ring systems provided products with very good diastereoselectivity and yield. The stereochemical outcome of the [5 + 2]-cycloaddition leading to 5- and 6-membered exocyclic rings can be rationalized using stereochemical models as shown in Fig. 3.

Treatment of substrate **9** with a base led to the expected aromatic oxidopyrylium zwitterion **11**, which contains a β-chiral center and an all carbon or an alkoxy alkyl tether bearing a terminal alkene. The cycloaddition leading to a five-membered exocyclic ring is proposed to proceed *via* transition-state **11A**, where the alkyl group occupies a pseudo-equatorial position on the envelope conformation of the developing five-membered ring.[45,46] The orientation of the substituent directs the approach of the terminal olefin from the bottom face, leading to the stereochemistry observed in cycloadducts **10a–c**. For cycloadditions forming six-membered exocyclic rings, the reaction would likely proceed through a thermodynamically more stable chair like transition-state **11B**, similar to that previously suggested by Wender and co-workers.[11] The alkyl or aryl β-substituents will occupy an equatorial position, leading to the approach of the alkene from the more favorable bottom face as shown. The formation of a chair-like transition-state leads to the stereochemical outcome observed in cycloadducts **10d–i**. The observed diastereoselectivity ranged from 3 : 1 to 10 : 1 (dr). The lower observed diastereoselectivity for the formation of the cyclohexane ring compared to the tetrahydropyran is possibly due to further stabilization of the six-membered transition state for alkoxy derivatives where *gauche* interactions are significantly less or absent. However, for the β-substituted cyclohexane ring, the developing *gauche* interaction destabilize transition-state **11B**. Interestingly, products with 7-membered rings (**10j** and **10k**) showed no diastereoselectivity. This is possibly due to the fact that the β-positioned alkyl or aryl substituent exerts no influence on the approach of the olefin from the top or bottom face in the flexible 7-membered ring transition-state.[47]

Conclusion

In summary, we investigated the diastereofacial selectivity associated with intramolecular [5 + 2]-cycloaddition reactions of substrates containing a β-chiral center on the alkene tether.

The reaction generates three new chiral centers in the 8-oxabicyclo(3.2.1)-octenone core with a high degree of diastereoselectivity for 5- and 6-membered fused carbocyclic and oxacyclic rings. For the formation of five-membered rings, increasing the size of β-substituents improved the degree of diastereoselectivity. The stereochemical outcome of this oxidopyrylium–alkene cycloaddition leading to a five-membered ring was rationalized using a transition-state model, where the substituent occupies a pseudo-equatorial position in an envelope conformation. The reaction with substrates leading to six-membered fused rings was rationalized using a model with a chair-like transition state, where the β-substituent occupies an equatorial position. Cycloaddition of substrates with an all-carbon tether bearing a β-methyl substitution resulted in excellent yield of the cycloadduct; however, the diastereoselectivity was moderate. Substrates containing an allyloxy tether, affording tetrahydropyran fused products, reacted with good to excellent diastereoselectivity. However, reactions with a homoallyloxy tether leading to 7-membered ring derivatives showed no diastereoselectivity, regardless of the size of the β-substitution. The reaction generally required longer times and product yields were moderate. Further investigation, including the application of the current methods for the synthesis of bioactive compounds, is in progress in our laboratories.

Experimental section

All chemicals were purchased from commercial suppliers unless otherwise stated. All reactions were carried out under an argon atmosphere in either flame or oven-dried (120 °C) glassware. Anhydrous organic solvents were obtained as follows. Tetrahydrofuran (THF) was freshly distilled from Na/benzophenone. *N*,*N*-Diisopropylethylamine (DIPEA), diisopropylamine (DIPA), and pyridine were distilled over calcium hydride. Isobutryaldehyde, ethyl acetate, acetone, benzaldehyde, pivalaldehyde, allyl bromide, and 2-furaldehyde were fractionally distilled. All other reagents were of reaction grade. Stainless steel syringes and cannulae were used to transfer air- or moisture-sensitive liquids. Thin-layer chromatography (TLC) analysis was conducted using glass backed silica gel plates (60 Å, 250 μm thick, F-254 indicator). Flash column chromatography was performed using a 230–400 mesh and 60 Å pore diameter silica gel. Organic solvents were removed under vacuum using a rotatory evaporator at 30 °C. ^{1}H and ^{13}C NMR spectra was obtained on a Bruker AV-III-400-HD, a Bruker AV-III-800, or an NEO500 instrument. ^{13}C NMR spectra were obtained at 100 and 125 MHz. Chemical shifts are reported in parts per million (ppm) with respect to the residual solvent peak. NMR data are reported as δ (chemical shift), *J*-value (Hz), integration, and splitting pattern, where s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, m = multiplet, dd = doublet of doublets and so on. High-resolution mass spectrometry (HRMS) spectra were recorded under positive electron spray ionization (ESI+) and positive atmospheric pressure chemical ionization (APCI+) conditions using an LTQ Orbitrap Mass Spectrometer at the Purdue University Department of Chemistry Mass Spectrometry Center.

(*E*)-1-(Furan-2-yl)but-2-en-1-one (12a)

To a solution of known (*E*)-1-(furan-2-yl)but-2-en-1-ol[48] (787.3 mg, 5.78 mmol) in Et_2O (18 mL), activated MnO_2 (3.02 g, 37.4 mmol) was added and the reaction was stirred for 26 h, filtered over Celite, and concentrated *in vacuo*. Enone **12a** (394.6 mg, 47% yield) was isolated as an amorphous white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.16 (dd, *J* = 3.5, 0.8 Hz, 1H), 7.08 (dq, *J* = 15.4, 6.9 Hz, 1H), 6.75 (dq, *J* = 15.4, 1.7 Hz, 1H), 6.48 (dd, *J* = 3.6, 1.7 Hz, 1H), 1.90 (dd, *J* = 6.9, 1.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.9, 153.1, 146.4, 144.1, 126.4, 117.3, 112.2, 22.5, 18.3. Experimental data are consistent with the data reported in the literature.[49]

(*E*)-1-(Furan-2-yl)-3-phenylprop-2-en-1-one (12b)

To a round bottom flask charged with known 1-(furan-2-yl)-3-hydroxy-3-phenylpropan-1-one[50] (3.33 g, 15.4 mmol) in CH_2Cl_2 (100 mL), MsCl (2.4 mL, 31.0 mmol) and Et_3N (8.6 mL, 61.7 mmol) were added dropwise sequentially and the reaction was stirred for 12.5 h. Upon completion, the reaction was quenched with saturated NH_4Cl solution. The organic layer was separated, and the aqueous layer was washed with CH_2Cl_2 (3×). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified *via* silica gel column chromatography (20% EtOAc/hexanes) to give α,β-unsaturated ketone **12b** (2.09 g, 68% yield) as an amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 15.8 Hz, 1H), 7.65 (ddd, *J* = 4.5, 2.0, 0.7 Hz, 3H), 7.49–7.39 (m, 4H), 7.33 (dd, *J* = 3.6, 0.8 Hz, 1H), 6.60 (dd, *J* = 3.6, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.4, 143.9, 130.5, 128.9, 128.4, 121.1, 117.4, 112.5. Experimental data are consistent with the data reported in the literature.[51]

(*E*)-1-(Furan-2-yl)-4-methylpent-2-en-1-one (12c)

The reaction was conducted according to the procedure described for **12b** with known β-hydroxy ketone[52] (475 mg, 2.61 mmol), CH_2Cl_2 (25 mL), MsCl (0.4 mL, 5.17 mmol), and Et_3N (1.4 mL, 10 mmol), and the mixture was reacted for 21 h. The crude mixture was purified *via* silica gel column chromatography (20% EtOAc/hexanes) to afford α,β-unsaturated ketone **12c** (344.0 mg, 80% yield) as an amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64–7.58 (m, 1H), 7.24–7.21 (m, 1H), 7.13 (dd, *J* = 15.5, 6.7 Hz, 1H), 6.74 (dd, *J* = 15.5, 1.5 Hz, 1H), 6.55 (dd, *J* = 3.6, 1.7 Hz, 1H), 2.55 (hd, *J* = 6.7, 1.4 Hz, 1H), 1.12 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 155.2, 153.3, 146.3, 122.0, 117.3, 112.2, 31.3, 21.2. Experimental data are consistent with the data reported in the literature.[53]

1-(Furan-2-yl)-3-methylhex-5-en-1-one (13a)

To a round bottom flask charged with **12a** (20.4 mg, 0.14 mmol) in dry CH_2Cl_2 (2 mL) at −78 °C under argon, $BF_3 \cdot OEt_2$ (25 μL, 0.20 mmol) was added dropwise and the mixture was stirred for 15 min. Allyltrimethylsilane (0.1 mL, 0.63 mmol) was added dropwise, and the reaction was stirred for 1 h, then warmed to 0 °C slowly and stirred for 29 h. Upon completion, the reaction was quenched with saturated $NaHCO_3$ solution. The organic layer was separated, and the aqueous layer was washed with CH_2Cl_2 (3×). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified *via* silica gel column chromatography (2% EtOAc/hexanes) to give the 1,4-addition product **13a** (9.6 mg, 39% yield) as a yellow oil along with the recovery of the starting material (12.5 mg, 61% recovery). ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 1.7, 0.8 Hz, 1H), 7.15 (dd, J = 3.6, 0.8 Hz, 1H), 6.50 (dd, J = 3.6, 1.7 Hz, 1H), 5.84–5.70 (m, 1H), 5.02 (dtd, J = 3.3, 2.2, 1.2 Hz, 1H), 4.99 (h, J = 1.0 Hz, 1H), 2.81 (dd, J = 15.4, 5.7 Hz, 1H), 2.59 (dd, J = 15.4, 8.2 Hz, 1H), 2.31–2.17 (m, 1H), 2.15–1.97 (m, 2H), 0.95 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.2, 153.0, 146.1, 136.5, 116.8, 116.5, 112.0, 44.8, 41.2, 29.5, 19.7. HRMS (ESI+) *m/z*: $[M + H]^+$ calcd $C_{11}H_{15}O_2$ 179.1067; found 179.1066.

(*E*)-4-(Furan-2-yl)hepta-1,5-dien-4-ol (15)

To CuBr·DMS (129.2 mg, 0.628 mmol) in THF (10 mL) at 0 °C, allylmagnesium bromide (1.25 mL, 1.0 M in hexanes, 1.25 mmol) was added dropwise, after which the suspension became black. The solution was stirred for 10 minutes and then cooled to −78 °C, and **12a** (76 mg, 0.52 mmol) in THF (2 mL) was cannulated into the prepared suspension. The reaction was stirred at −78 °C for 15 min, quenched with saturated NH_4Cl solution, and diluted with EtOAc. The solids were filtered off, the organic layer was separated, and the aqueous layer was washed with EtOAc (3×). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Purification *via* silica gel column chromatography (2% EtOAc/hexanes) afforded **13a** in trace amounts and **15** (60.4 mg, 68% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, J = 1.9, 0.9 Hz, 1H), 6.31 (dd, J = 3.2, 1.8 Hz, 1H), 6.21 (dd, J = 3.2, 0.9 Hz, 1H), 5.79–5.63 (m, 3H), 5.18–5.10 (m, 2H), 2.79–2.72 (m, 1H), 2.63–2.56 (m, 1H), 1.76–1.70 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 141.8, 133.8, 133.0, 125.6, 119.5, 110.1, 105.9, 72.9, 45.0, 17.7. HRMS (APCI+) *m/z*: $[M - OH]^+$ calcd $C_{11}H_{13}O_1$ 161.0961; found 161.0960.

1-(Furan-2-yl)-3-phenylhex-5-en-1-one (13b)

The reaction was conducted according to the procedure described for **13a** with **12b** (420.4 mg, 2.12 mmol), CH_2Cl_2 (20 mL), $BF_3{\cdot}OEt_2$ (0.75 mL, 6.08 mmol), and allyltrimethylsilane (1.9 mL, 12.0 mmol). The reaction was stirred for 65 h. The crude mixture was purified *via* silica gel column chromatography (3% EtOAc/hexanes) to give the 1,4-addition product **13b** (149 mg, 29% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (dd, J = 1.7, 0.8 Hz, 1H), 7.30–7.25 (m, 3H), 7.25–7.20 (m, 2H), 7.20–7.14 (m, 1H), 7.10 (dd, J = 3.6, 0.8 Hz, 1H), 6.48 (dd, J = 3.6, 1.7 Hz, 1H), 5.68 (ddt, J = 17.1, 10.0, 7.0 Hz, 1H), 5.03–4.92 (m, 2H), 3.45 (p, J = 7.2 Hz, 1H), 3.14 (dd, J = 7.2, 1.5 Hz, 2H), 2.49–2.42 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.2, 153.0, 146.2, 144.0, 136.2, 128.4, 127.6, 126.4, 117.0, 116.8, 112.2, 44.5, 40.9, 40.6. HRMS (ESI+) *m/z*: $[M + H]^+$ calcd $C_{16}H_{17}O_2$ 241.1223; found 241.1222.

1-(Furan-2-yl)-3-isopropylhex-5-en-1-one (13c)

The reaction was conducted according to the procedure described for **13a** with **12c** (329.6 mg, 2.01 mmol), CH_2Cl_2 (20 mL), $BF_3{\cdot}OEt_2$ (2.5 mL, 20.3 mmol), and allyltrimethylsilane (4.8 mL, 30.2 mmol). The reaction was stirred for 14.5 h. The crude mixture was purified *via* silica gel column chromatography (3% EtOAc/hexanes) to give the 1,4-addition product **13c** (209 mg, 50% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (dt, J = 2.0, 1.0 Hz, 1H), 6.32 (dd, J = 3.3, 1.8 Hz, 1H), 6.22 (t, J = 3.5 Hz, 1H), 5.75 (ddt, J = 17.1, 10.0, 7.1 Hz, 1H), 5.08–4.95 (m, 2H), 4.79–4.70 (m, 1H), 2.19–1.92 (m, 2H), 1.92–1.62 (m, 3H), 1.56–1.31 (m, 1H), 0.93–0.78 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 156.7, 141.8, 141.7, 137.9, 137.8, 115.8, 115.7, 110.0, 110.0, 106.0, 105.6, 66.4, 66.0, 39.7, 39.4, 36.3, 36.2, 35.5, 35.1, 29.4, 29.1, 19.2, 18.7, 18.5. HRMS (ESI+) *m/z*: $[M + H]^+$ calcd $C_{13}H_{19}O_2$ 207.1385; found 207.1280.

1-(Furan-2-yl)-3-methylhex-5-en-1-ol (14a)

A round bottom flask containing **13a** (37.7 mg, 0.208 mmol) in MeOH (3 mL) was charged with $NaBH_4$ (9 mg, 0.24 mmol) and the mixture was stirred for 2.5 h. The crude mixture was concentrated *in vacuo* and diluted with water and extracted with EtOAc (3×). Purification *via* silica gel column chromatography (5–10% EtOAc/hexanes) afforded furanol **14a** (32.2 mg, 86% yield) as a clear oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (td, J = 1.9, 0.8 Hz, 1H), 6.32 (dd, J = 3.2, 1.9 Hz, 1H), 6.22 (dq, J = 2.3, 0.7 Hz, 1H), 5.84–5.68 (m, 1H), 5.05–4.96 (m, 2H), 4.80–4.74 (m, 1H), 2.18–2.04 (m, 1H), 2.03–1.84 (m, 2H), 1.83–1.52 (m, 2H), 0.93 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 156.7, 141.9, 141.8, 136.9, 136.8, 116.1, 116.0, 110.0, 105.9, 105.5, 65.9, 65.5, 42.0, 42.0, 41.6, 40.9, 29.2, 29.0, 19.7, 18.9. HRMS (APCI+) *m/z*: $[M - OH]^+$ calcd $C_{11}H_{15}O_2$ 163.1117; found 163.1116.

1-(Furan-2-yl)-3-phenylhex-5-en-1-ol (14b)

The reaction was conducted (2.5 h) according to the procedure described for **14a** with **13b** (146.0 mg, 0.61 mmol) in a mixture of H_2O and THF (1 : 1) and $NaBH_4$ (128.5 mg, 3.40 mmol). Purification *via* silica gel column chromatography (5–10% EtOAc/hexanes) afforded furanol **14b** (124.4 mg, 64% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.27 (m, 3H), 7.24–7.18 (m, 2H), 7.13 (dd, J = 7.5, 1.1 Hz, 1H), 6.31 (ddd, J = 20.8, 3.2, 1.8 Hz, 1H), 6.16 (ddt, J = 12.5, 3.3, 0.7 Hz, 1H), 5.76–5.54 (m, 1H), 5.04–4.89 (m, 2H), 4.44 (ddd, J = 44.3, 9.3, 4.7 Hz, 1H), 3.09–2.49 (m, 1H), 2.49–2.19 (m, 3H), 2.19–1.95 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 155.9, 144.2, 142.1, 141.7, 136.5, 136.3, 128.4, 127.8, 127.5, 126.3, 116.2, 116.2, 110.0, 106.6, 105.3, 66.0, 65.1, 42.2, 41.6, 41.4, 41.1. HRMS (ESI+) *m/z*: $[M - OH]^+$ calcd $C_{16}H_{17}O_2$ 225.1274; found 225.1275.

1-(Furan-2-yl)-3-isopropylhex-5-en-1-ol (14c)

The reaction was conducted (2.3 h) according to the procedure described for **14a** with **13c** (166.5 mg, 0.81 mmol) in MeOH (8 mL) and 31.1 mg $NaBH_4$ (0.82 mmol). Purification *via* silica gel column chromatography (5–10% EtOAc/hexanes) afforded furanol **14c** (124.4 mg, 74% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (dt, *J* = 2.0, 1.0 Hz, 1H), 6.32 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.22 (t, *J* = 3.5 Hz, 1H), 5.75 (ddt, *J* = 17.1, 10.0, 7.1 Hz, 1H), 5.08–4.95 (m, 2H), 4.79–4.70 (m, 1H), 2.19–1.92 (m, 2H), 1.92–1.62 (m, 3H), 1.56–1.31 (m, 1H), 0.93–0.78 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 156.7, 141.8, 141.7, 137.9, 137.8, 115.8, 115.7, 110.0, 110.0, 106.0, 105.6, 66.4, 66.0, 39.7, 39.4, 36.3, 36.2, 35.5, 35.1, 29.4, 29.1, 19.2, 18.7, 18.5. HRMS (ESI+) *m*/*z*: $[M - OH]^+$ calcd $C_{13}H_{19}O_2$ 191.1430; found 191.1431

Methyl 3-methylhept-6-enoate (17)

To a round bottom flask charged with argon and activated magnesium turnings (1.76 g, 72.4 mmol), known ethyl (*Z*)-3-methylhepta-2,6-dienoate[54] (773 mg, 4.59 mmol) in methanol (50 mL) was added and the mixture was stirred for 4 h and then brought to vigorous reflux. Upon completion, the reaction was diluted with 200 mL Et_2O and extracted twice with 1 M HCl and once with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was passed through a silica plug to afford **17** (457 mg, 64% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 5.75 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.03–4.84 (m, 2H), 3.63 (d, *J* = 5.9 Hz, 3H), 2.41–1.73 (m, 4H), 1.39 (ddt, *J* = 15.6, 9.4, 6.1 Hz, 1H), 1.30–1.11 (m, 2H), 1.02–0.80 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 138.4, 114.4, 51.2, 41.4, 35.7, 31.0, 29.7, 19.4. HRMS (APCI+) *m*/*z*: $[M + H]^+$ calcd $C_{10}H_{19}O_2$ 157.1223; found 157.1223.

1-(Furan-2-yl)-3-methylhept-6-en-1-ol (18)

To a flame dried round bottom flask with ester **17** (169.9 mg, 1.09 mmol) in dry *n*-pentane (10 mL) at −78 °C, DIBAL (1.0 M in hexanes, 1.15 mL, 1.15 mmol) was added dropwise over 10 min. The reaction was stirred for an additional 20 min and quenched with methanol (0.05 mL) and stirred until the evolution of hydrogen ceased. Saturated aqueous Rochelle's salt (1.1 mL) was added dropwise and the reaction was slowly brought to 23 °C and stirred until the solution became gelatinous. The mixture was filtered over a mat of Na_2SO_4 and Celite and washed twice with *n*-pentanes (5 mL).

A solution of 2-lithiofuran was prepared by charging a dry round bottom flask with furan (0.25 mL, 3.43 mmol) in THF (10 mL) and cooled to 0 °C; then *n*-BuLi (1.1 mL, 1.42 M solution in hexanes) was added dropwise. The reaction was stirred for 30 min and then cooled to −78 °C. The crude aldehyde in *n*-pentanes as described above was cannulated into the prepared solution of 2-lithiofuran. The reaction was stirred for 15 min, quenched with saturated NH_4Cl, and warmed to 23 °C. The solution was diluted with EtOAc and the organic layers were separated. The aqueous layer was extracted with EtOAc (3×); the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Purification *via* silica gel column chromatography afforded furanol **18** (77.5 mg, 37% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (td, *J* = 1.7, 0.8 Hz, 1H), 6.31 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.21 (t, *J* = 2.6 Hz, 1H), 5.78 (dddt, *J* = 16.9, 10.2, 8.9, 6.6 Hz, 1H), 4.99 (ddd, *J* = 17.2, 6.4, 1.8 Hz, 1H), 4.95–4.88 (m, 1H), 4.74 (dd, *J* = 8.8, 5.4 Hz, 1H), 2.28–1.95 (m, 2H), 1.93–1.79 (m, 1H), 1.75–1.37 (m, 3H), 1.34–1.16 (m, 1H), 0.92 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 156.7, 141.8, 141.7, 138.9, 138.9, 114.2, 110.0, 105.8, 105.4, 65.9, 65.5, 42.6, 42.5, 36.5, 35.8, 31.0, 30.9, 28.9, 28.6, 19.8, 18.9. HRMS (APCI+) *m*/*z*: $[M - OH]^+$ calcd $C_{12}H_{17}O$ 177.1274; found 177.1276.

4-(Furan-2-yl)-4-hydroxy-1-phenylbutan-2-one (19e)

To a dried round bottom flask with dry CH_2Cl_2 (100 mL), phenyl acetone (2 mL, 14.5 mmol) was added and the mixture was cooled to −78 °C. DIPEA (3 mL, 17.2 mmol) and *tert*-butyldimethylsilyl triflate (4 mL, 17.4 mmol) were added dropwise sequentially. The reaction mixture was stirred at −78 °C for 15 min, and furfural (0.83 mL, 10 mmol) was added dropwise. Stirring of the reaction mixture was continued at −78 °C for 30 min; the mixture was then warmed to 0 °C after which it was stirred for an additional 1.5 h. The reaction mixture was poured over silica and the column was flushed with diethyl ether. The crude mixture was concentrated *in vacuo* and purification *via* silica gel column chromatography (1% EtOAc/hexanes, gravity pressure) afforded 4-((*tert*-butyldimethylsilyl)oxy)-4-(furan-2-yl)-1-phenylbutan-2-one in 60% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.13 (m, 7H), 6.28 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.14 (d, *J* = 3.2 Hz, 1H), 5.26–5.16 (m, 1H), 3.09 (dd, *J* = 15.7, 8.5 Hz, 1H), 2.73 (dd, *J* = 15.7, 4.6 Hz, 1H), 0.82 (s, 9H), 0.03 (s, 3H), −0.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 141.6, 133.6, 129.4, 128.6, 126.9, 110.0, 106.1, 64.8, 51.3, 48.6, 25.6, 25.3, 18.0, −5.2, −5.4. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{20}H_{28}O_3SiNa$ 367.1705; found 367.1703.

To a dry round bottom flask charged with the above siloxane and THF (40 mL) was added TBAF (15 mL, 1.0 M in THF) and the mixture was stirred for 15 min. The reaction was quenched with sat. NH_4Cl solution and extracted with EtOAc (3×). The combined organic layers were washed with brine and dried over Na_2SO_4 and then concentrated *in vacuo*. Product **19e** was isolated in 57% yield (16% alcohol elimination products were also isolated) *via* silica gel column chromatography. ^1H NMR (500 MHz, $CDCl_3$) δ 7.49–7.22 (m, 5H), 6.37 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.27 (d, *J* = 3.3 Hz, 1H), 5.20 (dd, *J* = 8.7, 3.7 Hz, 1H), 3.80 (s, 2H), 3.13 (dd, *J* = 17.6, 8.8 Hz, 1H), 2.99 (ddd, *J* = 17.7, 3.4, 1.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.1, 142.2, 133.4, 129.5, 128.9, 127.4, 110.3, 106.4, 63.9, 50.8, 46.6. HRMS (ESI+) *m*/*z*: $[M - OH]^+$ calcd $C_{14}H_{13}O_2$ 213.0910; found 213.0916.

4-(Furan-2-yl)-4-((tetrahydro-2*H*-pyran-2-yl)oxy)butan-2-one (20a)

A round bottom flask was charged with 4-(furan-2-yl)-4-hydroxybutan-2-one[50] (2.67 g, 17.3 mmol), 3,4-dihydro-2*H*-pyran

(3.1 mL, 34.0 mmol), and pyridinium *p*-toluenesulfonic acid (PPTS) (5.16 g, 20.5 mmol) in CH_2Cl_2 (170 mL) and the mixture was stirred for 19 h. The reaction was quenched with saturated $NaHCO_3$, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Purification *via* silica gel column chromatography (8–10% EtOAc/hexanes) afforded **20a** (3.71 g, 90% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.30–7.27 (m, 1H), 6.27–6.19 (m, 2H), 5.05 (dd, J = 8.4, 5.0 Hz, 1H), 4.77 (t, J = 3.5 Hz, 1H), 3.54 (ddd, J = 11.7, 9.0, 3.2 Hz, 1H), 3.31–3.25 (m, 1H), 3.10 (dd, J = 16.5, 8.3 Hz, 1H), 2.76 (dd, J = 16.6, 5.0 Hz, 1H), 2.09 (s, 3H), 1.73–1.32 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.9, 154.5, 141.9, 110.2, 107.1, 98.7, 68.6, 62.0, 47.5, 30.8, 30.5, 25.3, 19.1. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{13}H_{18}O_4Na$ 289.1416; found 289.1404.

3-(Furan-2-yl)-1-phenyl-3-((tetrahydro-2*H*-pyran-2-yl)oxy)propan-1-one (20b)

The reaction was conducted according to the procedure described for **20a** with 3-(furan-2-yl)-3-hydroxy-1-phenylpropan-1-one (2.04 g, 9.42 mmol), 3,4-dihydro-2*H*-pyran (1 mL, 11.0 mmol), and PPTS (5.24 g, 20.9 mmol) in CH_2Cl_2 (90 mL) and stirred for 72 h. Purification *via* silica gel column chromatography (10% EtOAc/hexanes) afforded **20b** (2.01 g, 71% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 8.03–7.95 (m, 2H), 7.60–7.52 (m, 1H), 7.50–7.42 (m, 2H), 7.38 (ddd, J = 5.0, 2.4, 1.3 Hz, 1H), 6.38–6.28 (m, 2H), 5.39 (ddd, J = 35.1, 7.9, 5.0 Hz, 1H), 4.74 (dt, J = 165.7, 3.2 Hz, 1H), 3.83–3.70 (m, 2H), 3.66–3.43 (m, 1H), 3.34 (ddt, J = 16.8, 8.9, 3.2 Hz, 2H), 2.19–2.02 (m, 2H), 1.72 (t, J = 8.4 Hz, 1H), 1.66–1.36 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 154.8, 152.9, 142.6, 142.0, 137.3, 137.1, 133.2, 133.1, 128.6, 128.6, 128.3, 128.2, 110.2, 110.1, 109.0, 107.1, 99.1, 94.7, 69.0, 66.4, 62.1, 61.8, 43.0, 30.9, 30.5, 30.3, 25.4, 25.3, 19.2, 18.9. HRMS (ESI+) *m*/*z*: $[M + H]^+$ calcd $C_{18}H_{21}O_4$ 301.1434; found 301.1440.

1-(Furan-2-yl)-4-methyl-1-((tetrahydro-2*H*-pyran-2-yl)oxy)pentan-3-one (20c)

The reaction was conducted according to the procedure described for **20a** with 1-(furan-2-yl)-1-hydroxy-4-methylpentan-3-one (2.63 g, 14.4 mmol), 3,4-dihydro-2*H*-pyran (2.6 mL, 28.5 mmol), and PPTS (3.98 g, 15.8 mmol) in CH_2Cl_2 (150 mL) and stirred for 25 h. Purification *via* silica gel column chromatography (8% EtOAc/hexanes) afforded **19c** (3.17 g, 83% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.39–7.33 (m, 1H), 6.33–6.22 (m, 2H), 5.20 (ddd, J = 51.1, 8.4, 5.0 Hz, 1H), 4.96–4.79 (m, 1H), 4.51 (s, 0H), 3.84 (ddd, J = 21.5, 11.6, 5.4 Hz, 2H), 3.63–3.31 (m, 3H), 3.26–3.18 (m, 1H), 2.85–2.78 (m, 1H), 2.61 (dhept, J = 21.0, 7.0 Hz, 1H), 1.91–1.40 (m, 7H), 1.13–1.06 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.8, 211.5, 154.8, 152.8, 142.5, 141.9, 110.2, 110.1, 109.0, 107.0, 99.2, 94.7, 94.5, 69.0, 65.9, 63.0, 62.1, 61.7, 44.6, 44.5, 41.8, 41.6, 30.7, 30.6, 30.3, 25.5, 25.4, 25.3, 19.8, 19.2, 18.9, 17.8, 17.8, 17.7. HRMS (ESI+) *m*/*z*: $[M + H]^+$ calcd $C_{13}H_{19}O_4$ 289.1416; found 289.1404.

1-(Furan-2-yl)-4,4-dimethyl-1-((tetrahydro-2*H*-pyran-2-yl)oxy)pentan-3-one (20d)

The reaction was conducted according to the procedure described for **20a** with 1-(furan-2-yl)-1-hydroxy-4,4-dimethylpentan-3-one (221.9 mg, 1.13 mmol), 3,4-dihydro-2*H*-pyran (1.0 mL, 11.0 mmol), and PPTS (309 mg, 1.23 mmol) in CH_2Cl_2 (10 mL) and stirred for 13.5 h. Purification *via* silica gel column chromatography (15% EtOAc/hexanes) afforded **20d** (306 mg, 96% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.32 (m, 1H), 6.32–6.24 (m, 2H), 5.23 (ddd, J = 59.4, 8.2, 5.3 Hz, 1H), 4.96–4.48 (m, 1H), 3.90–3.80 (m, 1H), 3.60–3.48 (m, 1H), 3.35–3.24 (m, 1H), 2.83 (ddd, J = 32.7, 16.8, 5.3 Hz, 1H), 1.91–1.37 (m, 4H), 1.12 (d, J = 3.0 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.9, 212.4, 155.0, 152.8, 142.4, 141.8, 110.2, 110.0, 109.1, 107.0, 99.4, 94.7, 94.4, 69.2, 65.9, 62.9, 62.1, 61.7, 44.4, 44.3, 41.3, 41.1, 30.7, 30.6, 30.3, 26.0, 25.9, 25.5, 25.4, 25.3, 19.8, 19.2, 19.0. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{16}H_{24}O_4Na$ 303.1572; found 303.1559.

4-(Furan-2-yl)-1-phenyl-4-((tetrahydro-2*H*-pyran-2-yl)oxy)butan-2-one (20e)

The reaction was conducted (21 h) according to the procedure described for **20a** with **19e** (397.6 mg, 1.73 mmol), 3,4-dihydro-2*H*-pyran (0.19 mL, 2.08 mmol), and PPTS (435 mg, 1.73 mmol). Purification *via* silica gel column chromatography (15% EtOAc/hexanes) afforded **20e** (416 mg, 76% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.14 (m, 7H), 6.32–6.19 (m, 2H), 5.19 (ddd, J = 53.4, 8.4, 5.2 Hz, 1H), 4.84–4.47 (m, 1H), 3.86–3.30 (m, 4H), 3.20 (ddd, J = 16.4, 8.4, 2.7 Hz, 1H), 2.84 (ddd, J = 15.9, 5.3, 2.8 Hz, 1H), 1.79–1.39 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.5, 205.3, 154.4, 152.5, 142.6, 142.0, 133.8, 133.7, 129.6, 129.5, 128.9, 128.8, 128.7, 127.1, 127.1, 110.2, 110.1, 109.0, 107.2, 99.0, 94.8, 68.7, 66.1, 62.1, 62.0, 51.1, 51.0, 46.1, 46.1, 30.5, 30.3, 25.4, 25.3, 19.2, 19.1. HRMS (APCI+) *m*/*z*: $[M + Na]^+$ calcd $C_{19}H_{22}O_4Na$ 337.1410; found 337.1416.

2-(3-(Allyloxy)-1-(furan-2-yl)butoxy)tetrahydro-2*H*-pyran (21a)

A round-bottom flask was charged with **20a** (67.2 mg, 0.28 mmol) and $NaBH_4$ (35.8 mg, 0.94 mmol) in MeOH (3 mL) and the mixture was stirred for 1 h. The reaction was quenched with sat. NH_4Cl and diluted with EtOAc, and the layers were separated. The aqueous layer was extracted with EtOAc (3×); the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Purification *via* silica gel column chromatography (25% EtOAc/hexanes) afforded 4-(furan-2-yl)-4-((tetrahydro-2*H*-pyran-2-yl)oxy)butan-2-ol (60.1 mg, 89% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (ddt, J = 3.7, 1.9, 0.9 Hz, 1H), 6.37 (tt, J = 2.1, 1.3 Hz, 1H), 6.33 (d, J = 3.3 Hz, 1H), 5.01–4.85 (m, 2H), 4.11–3.89 (m, 1H), 3.73 (dddd, J = 36.5, 11.8, 8.6, 3.3 Hz, 1H), 3.49–3.34 (m, 1H), 2.59 (s, 2H), 2.24–2.07 (m, 1H), 2.01–1.46 (m, 7H), 1.26 (ddd, J = 6.2, 3.2, 1.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 142.0, 141.8, 110.1, 107.1, 106.6, 98.5, 72.6, 70.1, 66.6, 64.7, 62.6, 62.2, 42.7, 42.3, 30.8, 30.6, 25.3, 23.8, 23.6, 19.5, 19.3. HRMS (ESI+) *m*/*z*: $[M + H]^+$ calcd $C_{13}H_{21}O_4$ 241.1434; found 241.1413.

To the above alcohol (44.7 mg, 0.19 mmol) in DMF (2 mL), TBAI (7.3 mg, 19.8 μmol), NaH (54.5 mg, 60 wt% in mineral oil, 1.36 mmol), and allyl bromide (160 μL, 1.85 mmol) were added sequentially. The reaction was warmed to 50 °C and stirred for 16 h. The solution was diluted with EtOAc and the organic layers were separated. The aqueous layer was extracted with EtOAc (3×); the combined organic layers were washed with ice and brine sequentially, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified *via* silica gel column chromatography (8% EtOAc/hexanes) to give **21a** (28 mg, 53% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.39 (m, 1H), 6.40–6.27 (m, 2H), 6.04–5.87 (m, 1H), 5.30 (dddd, *J* = 19.3, 17.3, 6.0, 1.7 Hz, 1H), 5.18 (ddd, *J* = 18.2, 10.3, 1.6 Hz, 1H), 5.01–4.80 (m, 2H), 4.18–3.28 (m, 5H), 2.31 (dt, *J* = 14.1, 7.2 Hz, 0H), 2.25–2.10 (m, 1H), 2.07–1.81 (m, 2H), 1.75–1.44 (m, 4H), 1.27–1.18 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 155.2, 154.3, 153.8, 142.4, 142.3, 141.9, 141.7, 135.5, 135.3, 116.6, 116.4, 116.3, 110.0, 109.9, 108.8, 108.2, 107.3, 106.6, 99.0, 98.0, 95.0, 72.0, 71.9, 71.7, 71.3, 69.9, 69.7, 69.6, 69.6, 69.5, 69.4, 67.4, 66.6, 62.2, 41.9, 41.7, 41.5, 41.0, 30.8, 30.7, 30.5, 25.5, 25.4, 20.0, 19.9, 19.7, 19.5, 19.4, 19.3. HRMS (ESI+) *m*/*z*: $[M - OAllyl]^+$ calcd $C_{13}H_{19}O_3$ 223.1329; found 223.1328.

2-(3-(Allyloxy)-1-(furan-2-yl)-3-phenylpropoxy)tetrahydro-2*H*-pyran (21b)

The reaction was conducted according to the procedure described for **21a** with **20b** (2.01 g, 6.71 mmol) and $NaBH_4$ (508 mg, 13.4 mmol) in MeOH (70 mL), and the mixture was reacted for 30 min. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded 3-(furan-2-yl)-1-phenyl-3-((tetrahydro-2*H*-pyran-2-yl)oxy)propan-1-ol (1.53 g, 75% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.29 (m, 5H), 7.28–7.21 (m, 1H), 6.35–6.23 (m, 2H), 5.09 (ddd, *J* = 17.5, 10.1, 4.0 Hz, 1H), 4.96–4.80 (m, 1H), 4.77–4.56 (m, 1H), 4.05–3.91 (m, 1H), 3.81 (d, *J* = 28.4 Hz, 1H), 3.73–3.27 (m, 1H), 2.50–2.30 (m, 1H), 2.22–2.05 (m, 1H), 1.89–1.41 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 154.2, 153.1, 144.2, 144.1, 142.5, 142.3, 141.9, 128.4, 128.2, 127.4, 127.2, 127.0, 125.6, 125.6, 110.0, 109.9, 108.4, 107.4, 107.3, 98.7, 98.3, 95.6, 73.4, 72.4, 72.0, 70.7, 70.2, 69.5, 68.2, 64.5, 62.7, 62.1, 53.3, 43.5, 43.1, 43.0, 30.9, 30.7, 30.3, 25.1, 20.8, 19.5, 19.2.

To the above alcohol (1.53 g, 5.06 mmol) in DMF (50 mL), NaH (1.05 g, 60 wt% in mineral oil, 26.3 mmol) and allyl bromide (4.3 mL, 49.7 mmol) were added sequentially. The reaction was stirred for 18 h. The solution was diluted with EtOAc and the organic layers were separated. The aqueous layer was extracted with EtOAc (3×); the combined organic layers were washed with ice and brine sequentially, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified *via* silica gel column chromatography (6% EtOAc/hexanes) to give **21b** (1.56 g, 90% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (ddd, *J* = 4.0, 1.9, 0.9 Hz, 1H), 7.37–7.23 (m, 6H), 6.36–6.21 (m, 2H), 5.98–5.77 (m, 1H), 5.31–5.00 (m, 3H), 4.95–4.72 (m, 1H), 4.65–4.47 (m, 1H), 4.13 (ddd, *J* = 8.9, 4.8, 1.8 Hz, 1H), 3.95–3.59 (m, 3H), 3.57–3.30 (m, 1H), 2.53–2.40 (m, 1H), 2.33–2.10 (m, 1H), 1.94–1.40 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 142.4, 141.9, 134.9, 128.4, 128.2, 127.4, 126.7, 126.5, 116.3, 109.8, 109.0, 95.1, 94.8, 78.2, 69.4, 67.5, 62.1, 42.7, 30.6, 30.4, 25.4, 19.2. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{21}H_{26}O_4Na$ 365.1723; found 365.1728.

2-((3-(Allyloxy)-1-(furan-2-yl)-4-methylpentyl)oxy)tetrahydro-2*H*-pyran (21c)

The reaction was conducted according to the procedure described for **21a** with **20c** (3.17 g, 11.9 mmol) and $NaBH_4$ (692 mg, 18.3 mmol) in MeOH (100 mL) and stirred for 1.5 h. Purification *via* silica gel column chromatography (25% EtOAc/hexanes) afforded 1-(furan-2-yl)-4-methyl-1-((tetrahydro-2*H*-pyran-2-yl)oxy)pentan-3-ol (2.32 g, 83% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (ddd, *J* = 7.8, 1.9, 0.9 Hz, 1H), 6.37–6.24 (m, 2H), 5.00–4.82 (m, 2H), 3.75–3.56 (m, 1H), 3.43–3.30 (m, 2H), 2.82 (s, 1H), 2.48 (s, 0H), 2.14–1.94 (m, 2H), 1.87–1.42 (m, 6H), 1.00–0.86 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 155.0, 141.9, 141.6, 110.1, 107.2, 106.5, 98.7, 98.3, 74.8, 72.8, 70.3, 62.4, 62.0, 37.9, 37.7, 34.0, 33.9, 30.8, 30.6, 25.3, 25.3, 19.4, 19.2, 18.6, 18.3, 17.6, 17.5. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{15}H_{24}O_4Na$ 291.1567; found 291.1566.

To the above alcohol (2.32 g, 8.63 mmol) in DMF (80 mL), NaH (3.51 g, 60 wt% in mineral oil, 87.8 mmol) and allyl bromide (7.5 mL, 86.7 mmol) were added sequentially, and the reaction was stirred for 22 h. The solution was diluted with EtOAc and the organic layers were separated. The aqueous layer was extracted with EtOAc (3×); the combined organic layers were washed with ice and brine sequentially, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified *via* silica gel column chromatography (6% EtOAc/hexanes) to give **21c** (2.2 g, 83% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.31 (m, 1H), 6.32–6.19 (m, 3H), 5.96–5.79 (m, 1H), 5.27–5.04 (m, 3H), 4.93–4.45 (m, 3H), 4.07–3.72 (m, 4H), 3.67–3.24 (m, 3H), 2.92–2.81 (m, 1H), 2.08–1.38 (m, 10H), 0.93–0.78 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 155.1, 154.7, 153.7, 142.4, 142.1, 141.9, 141.5, 135.7, 135.5, 135.4, 135.4, 116.3, 116.0, 116.0, 110.0, 110.0, 109.8, 109.2, 107.9, 107.5, 106.5, 99.1, 97.9, 95.5, 94.8, 80.7, 80.3, 80.0, 70.9, 70.8, 70.7, 70.5, 70.4, 70.2, 67.8, 67.3, 62.6, 62.1, 62.0, 62.0, 35.7, 35.2, 34.9, 34.5, 30.9, 30.8, 30.7, 30.4, 30.4, 30.4, 30.0, 25.5, 25.4, 25.4, 19.7, 19.4, 19.3, 19.2, 18.3, 18.2, 18.0, 17.3, 17.2, 17.0, 17.0. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{13}H_{20}O_3Na$ 331.1885; found 331.1873.

2-((3-(Allyloxy)-1-(furan-2-yl)-4,4-dimethylpentyl)oxy)tetrahydro-2*H*-pyran (21d)

The reaction was conducted according to the procedure described for **21a** with **20d** (306 mg, 1.09 mmol) and $NaBH_4$ (96 mg, 2.54 mmol) in MeOH (10 mL) for 3 h. Purification of the product *via* silica gel column chromatography (25% EtOAc/hexanes) afforded 1-(furan-2-yl)-4,4-dimethyl-1-((tetrahydro-2*H*-pyran-2-yl)oxy)pentan-3-ol (222.9 mg, 72% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.40 (m, 1H), 6.40–6.29

(m, 2H), 5.08–4.84 (m, 1H), 4.60–4.55 (m, 0H), 4.21–3.93 (m, 1H), 3.81–3.24 (m, 2H), 2.20–1.52 (m, 6H), 0.96 (ddd, *J* = 9.7, 6.5, 1.1 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 153.5, 142.5, 142.3, 142.0, 141.7, 110.1, 110.0, 108.5, 107.3, 107.1, 106.5, 98.8, 98.6, 95.4, 79.0, 74.4, 70.9, 69.1, 64.9, 62.7, 36.0, 35.6, 34.8, 34.4, 31.0, 30.6, 30.3, 25.9, 25.8, 25.7, 25.6, 25.5, 25.3, 25.2, 21.0, 19.6. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{16}H_{26}O_4$ 305.1729; found 305.1714.

To the above alcohol (202 mg, 0.72 mmol) in DMF (8 mL), NaH (286 mg, 60 wt% in mineral oil, 7.16 mmol) and allyl bromide (0.6 mL, 6.93 mmol) were added sequentially and warmed to 50 °C. The reaction was stirred for 16 h. The solution was diluted with EtOAc and the organic layers were separated. The aqueous layer was extracted with EtOAc (3×); the combined organic layers were washed with ice and brine sequentially, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified *via* silica gel column chromatography (6% EtOAc/hexanes) to give **21d** (189 mg, 82% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.34 (m, 1H), 6.35–6.22 (m, 2H), 5.98–5.85 (m, 1H), 5.25 (ddq, *J* = 17.2, 6.7, 1.8 Hz, 1H), 5.14–5.07 (m, 1H), 4.93–4.71 (m, 2H), 4.53–4.23 (m, 1H), 4.08–3.86 (m, 3H), 3.70–3.16 (m, 2H), 2.65 (ddd, *J* = 12.0, 9.6, 2.1 Hz, 1H), 2.29–2.11 (m, 2H), 2.05–1.39 (m, 7H), 0.94–0.84 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.1, 155.1, 154.9, 153.6, 142.5, 142.1, 142.0, 141.6, 135.8, 135.5, 135.5, 135.3, 116.0, 115.8, 115.7, 115.7, 110.1, 110.0, 109.9, 109.9, 109.5, 107.8, 106.7, 98.8, 97.9, 96.5, 94.7, 85.1, 84.6, 84.4, 74.3, 74.2, 73.9, 73.8, 71.2, 70.7, 68.6, 68.1, 63.5, 62.3, 62.1, 62.0, 37.0, 36.5, 36.1, 36.0, 35.9, 35.9, 35.8, 31.0, 30.9, 30.8, 30.4, 26.4, 26.4, 26.2, 26.2, 25.5, 25.4, 25.3, 20.3, 19.6, 19.4, 19.2.

2-(3-(Allyloxy)-1-(furan-2-yl)-4-phenylbutyl)tetrahydro-2*H*-pyran (21e)

The reaction was conducted according to the procedure described for **21a** with **20e** (700.8 mg, 2.23 mmol) and $NaBH_4$ (168 mg, 4.44 mmol) in MeOH (20 mL) for 1.5 h. Purification *via* silica gel column chromatography (25% EtOAc/hexanes) afforded 1-(furan-2-yl)-4,4-dimethyl-1-((tetrahydro-2*H*-pyran-2-yl)oxy)pentan-3-ol (551.2 mg, 78% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dtd, *J* = 4.6, 2.3, 1.3 Hz, 1H), 6.35–6.23 (m, 2H), 5.02–4.49 (m, 2H), 4.22–3.83 (m, 2H), 3.77–3.27 (m, 1H), 2.19–2.02 (m, 2H), 1.95–1.61 (m, 1H), 1.53 (tdd, *J* = 11.5, 7.8, 4.3 Hz, 4H), 1.21 (td, *J* = 6.4, 2.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 110.0, 109.9, 108.1, 98.3, 95.5, 70.3, 68.3, 67.2, 64.6, 62.6, 42.6, 42.5, 30.2, 25.1, 23.3, 22.6, 19.5. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{19}H_{24}O_4Na$ 339.1572; found 339.1571.

To the above alcohol (33.6 mg, 0.106 mmol) in DMF (2 mL), NaH (59.3 mg, 60 wt% in mineral oil, 1.48 mmol) and allyl bromide (140 μL, 1.03 mmol) were added sequentially and warmed to 50 °C. The reaction was stirred for 14 h. The solution was diluted with EtOAc and the organic layers were separated. The aqueous layer was extracted with EtOAc (3×), the combined organic layers were washed with ice and brine sequentially, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified *via* silica gel column chromatography (8% EtOAc/hexanes) to give **21e** (30.5 mg, 81% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.18 (m, 5H), 6.39–6.16 (m, 2H), 5.98–5.80 (m, 1H), 5.45–5.12 (m, 2H), 4.99 (td, *J* = 6.4, 2.9 Hz, 1H), 4.91–4.78 (m, 1H), 4.55 (dt, *J* = 16.9, 3.5 Hz, 1H), 4.33–3.33 (m, 5H), 2.97–2.75 (m, 2H), 2.27–2.07 (m, 2H), 2.01–1.47 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 142.3, 135.0, 129.5, 128.2, 128.1, 126.0, 116.3, 109.7, 108.7, 95.0, 70.5, 70.4, 67.3, 62.1, 40.6, 38.8, 30.4, 25.4, 19.2. HRMS (ESI+) *m*/*z*: $[M - OAllyl]^+$ calcd $C_{19}H_{23}O_3$ 299.1647; found 299.1637.

3-(Allyloxy)-1-(furan-2-yl)butan-1-ol (22a)

To a round bottom flask charged with **21a** (1.82 g, 6.49 mmol) in MeOH (65 mL), DOWEX-50W-X8 (2.72 g) was added, and the reaction was stirred for 7 h. The resin was filtered off, and the crude mixture was concentrated under reduced pressure. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded alcohol **22a** (455 mg, 36% yield) as a yellow oil along with the recovery of the starting material (655 mg, 36% recovery). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.38 (m, 1H), 6.37 (td, *J* = 3.4, 1.8 Hz, 1H), 6.29 (t, *J* = 3.7 Hz, 1H), 5.97 (dddt, *J* = 19.3, 10.8, 5.6, 3.0 Hz, 1H), 5.37–5.27 (m, 1H), 5.26–5.20 (m, 1H), 5.00 (ddd, *J* = 31.4, 8.6, 3.5 Hz, 1H), 4.23–4.10 (m, 1H), 4.00–3.92 (m, 1H), 3.80 (dqd, *J* = 9.4, 5.9, 3.3 Hz, 1H), 2.18–1.94 (m, 2H), 1.26 (dd, *J* = 6.2, 2.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 156.5, 141.8, 141.7, 134.9, 134.6, 117.2, 116.9, 110.1, 105.5, 75.1, 72.8, 69.6, 69.3, 67.5, 65.6, 42.6, 41.5, 19.7, 19.4. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{11}H_{216}O_3Na$ 219.0997; found 219.0999.

3-(Allyloxy)-1-(furan-2-yl)-3-phenylpropan-1-ol (22b)

The reaction was conducted according to the procedure described for **22a** with **21b** (766 mg, 2.24 mmol) and DOWEX-50W-X8 (1.2 g) in MeOH (22 mL) for 6 h. Purification *via* silica gel column chromatography (8–12% EtOAc/hexanes) afforded alcohol **22b** (318 mg, 36% yield) as a yellow oil along with the recovery of the starting material (318 mg, 55% recovery). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.27 (m, 6H), 6.32 (ddd, *J* = 11.4, 3.2, 1.8 Hz, 1H), 6.25 (t, *J* = 3.9 Hz, 1H), 5.90 (dddd, *J* = 16.8, 10.3, 6.2, 5.0 Hz, 1H), 5.25 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.21–5.14 (m, 1H), 4.95 (ddd, *J* = 33.9, 8.8, 3.4 Hz, 1H), 4.59 (ddd, *J* = 13.7, 9.5, 3.8 Hz, 1H), 3.94 (ddt, *J* = 12.7, 5.1, 1.6 Hz, 1H), 3.83–3.74 (m, 1H), 2.45–2.25 (m, 1H), 2.22–2.09 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 156.4, 141.8, 141.8, 141.7, 141.3, 134.6, 134.3, 128.7, 128.6, 128.0, 127.8, 126.6, 126.5, 117.3, 117.1, 110.2, 110.2, 105.8, 105.7, 81.1, 78.6, 69.8, 69.5, 67.1, 65.3, 43.9, 43.4. HRMS (APCI+) *m*/*z*: $[M - OH]^+$ calcd $C_{16}H_{17}O_2$ 241.1223; found 241.1216.

3-(Allyloxy)-1-(furan-2-yl)-4-methylpentan-1-ol (22c)

The reaction was conducted according to the procedure described for **22a** with **21c** (61.6 mg, 0.2 mmol) and DOWEX-50W-X8 (108.8 mg) in MeOH (2 mL) for 1.5 h. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded alcohol **22c** (18.5 mg, 47% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, J = 1.9, 0.9 Hz, 1H), 6.38 (d, J = 1.4 Hz, 1H), 6.32–6.28 (m, 1H), 6.05–5.93 (m, 1H), 5.34 (ddt, J = 17.2, 5.6, 1.6 Hz, 1H), 5.28–5.18 (m, 1H), 4.99 (ddd, J = 37.6, 8.5, 3.7 Hz, 1H), 4.21–4.10 (m, 1H), 4.05–3.94 (m, 1H), 3.47 (dddd, J = 19.1, 8.7, 4.8, 3.1 Hz, 1H), 2.15–1.92 (m, 3H), 1.03–0.90 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 141.8, 135.0, 134.6, 117.2, 116.9, 110.1, 105.6, 105.5, 84.0, 81.6, 70.9, 70.2, 67.9, 65.6, 35.0, 34.8, 30.1, 29.6, 18.8, 18.5, 17.1, 16.2. HRMS (ESI+) *m/z*: $[M + Na]^+$ calcd $C_{13}H_{20}O_3Na$ 247.1310; found 247.1302.

3-(Allyloxy)-1-(furan-2-yl)-4,4-dimethylpentan-1-ol (22d)

The reaction was conducted according to the procedure described for **22a** with **21d** (188.5 mg, 0.58 mmol) and DOWEX-50W-X8 (1.02 g) in MeOH (6 mL) for 4.5 h. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded alcohol **22d** (47.6 mg, 34% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (ddt, J = 2.8, 1.8, 0.9 Hz, 1H), 6.39 (ddt, J = 4.9, 3.0, 1.3 Hz, 1H), 6.34–6.27 (m, 1H), 6.07–5.93 (m, 1H), 5.40–5.28 (m, 1H), 5.21 (dddd, J = 10.4, 9.0, 2.3, 1.0 Hz, 1H), 4.95 (td, J = 8.5, 4.1 Hz, 1H), 4.26–4.10 (m, 2H), 3.39–3.09 (m, 1H), 2.18–2.12 (m, 1H), 2.11–1.98 (m, 1H), 1.91 (dddd, J = 14.3, 10.4, 2.8, 0.8 Hz, 0H), 0.98 (dd, J = 10.8, 0.8 Hz, 10H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.4, 156.5, 141.9, 141.8, 135.4, 134.7, 116.7, 116.2, 110.2, 106.0, 105.5, 87.5, 84.5, 74.5, 74.3, 67.3, 65.2, 37.1, 36.5, 36.3, 35.9, 26.4, 26.2. HRMS (ESI+) *m/z*: $[M + Na]^+$ calcd $C_{14}H_{22}O_3Na$ 261.1467; found 261.1459.

3-(Allyloxy)-1-(furan-2-yl)-4-phenylbutan-1-ol (22e)

The reaction was conducted according to the procedure described for **22a** with **21e** (375 mg, 1.05 mmol) and DOWEX-50W-X8 (567.6 mg) in MeOH (10 mL) for 24 h. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded alcohol **22e** (214.6 mg, 75% yield) as a yellow oil along with the recovery of the starting material with a mixture of side products. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.20 (m, 5H), 6.35–6.32 (m, 1H), 6.21 (dt, J = 3.2, 0.8 Hz, 1H), 5.86 (ddt, J = 17.1, 10.1, 6.8 Hz, 1H), 5.21–5.11 (m, 2H), 4.90 (dd, J = 8.8, 3.9 Hz, 1H), 3.87–3.74 (m, 2H), 3.52 (dt, J = 8.9, 6.6 Hz, 1H), 3.05 (dd, J = 13.6, 4.9 Hz, 1H), 2.78 (dd, J = 13.6, 7.5 Hz, 1H), 2.10–1.92 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 141.8, 137.8, 134.9, 129.5, 128.5, 126.5, 117.2, 110.1, 105.6, 81.4, 68.6, 67.6, 40.5, 39.6, 34.5, 29.3. HRMS (APCI+) *m/z*: $[M - OH]^+$ calcd $C_{17}H_{19}O_2$ 255.1380; found 255.1383.

Ethyl 3-(allyloxy)butanoate (24a)

A round bottom flask was charged with commercially available ethyl 3-hydroxybutanoate **23a** (2 mL, 15.4 mmol) and CH_2Cl_2 (45 mL) and the mixture was cooled to 0 °C. *O*-Allyl 2,2,2-trichloroacetimidate (6.8 mL, 44.8 mmol) and TfOH (0.1 mL, 1.13 mmol) were added sequentially. The reaction was stirred at 0 °C for 30 min and then warmed to 23 °C and stirred for 15 h. Purification *via* silica gel column chromatography (2% EtOAc/hexanes) afforded allyloxy **24a** (1.96 g, 74% yield) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.92 (ddt, J = 17.2, 10.3, 5.6 Hz, 1H), 5.33–5.13 (m, 2H), 4.17 (q, J = 7.1 Hz, 2H), 4.11–3.89 (m, 3H), 2.62 (dd, J = 15.0, 7.1 Hz, 1H), 2.40 (dd, J = 15.0, 5.9 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H), 1.24 (d, J = 6.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 135.1, 116.7, 71.8, 69.8, 60.4, 42.1, 19.9, 14.2. Experimental data are consistent with the data reported in the literature.[33]

Ethyl 3-(allyloxy)-3-phenylpropanoate (24b)

The reaction was conducted according to the procedure described for **24a** with commercially available ethyl 3-hydroxy-3-phenylpropanoate **23b** (1.75 mL, 10.1 mmol), *O*-allyl 2,2,2-trichloroacetimidate (3 mL, 19.8 mmol), and TfOH (0.1 mL, 1.13 mmol) in CH_2Cl_2 and pentanes (300 mL, 1 : 2) for 1.5 h. Purification *via* silica gel column chromatography (2% EtOAc/hexanes) afforded allyloxy **24b** (2.24 g, 52% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H), 5.87 (dddd, J = 17.3, 10.4, 6.1, 5.1 Hz, 1H), 5.21 (dq, J = 17.2, 1.7 Hz, 1H), 5.14 (dd, J = 10.4, 1.6 Hz, 1H), 4.81 (dd, J = 9.1, 4.9 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.92 (ddt, J = 12.7, 5.2, 1.5 Hz, 1H), 3.79 (ddt, J = 12.7, 6.1, 1.4 Hz, 1H), 2.83 (dd, J = 15.3, 9.1 Hz, 1H), 2.59 (dd, J = 15.2, 4.9 Hz, 1H), 1.23 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 140.9, 134.6, 128.6, 128.0, 126.7, 116.9, 77.7, 69.7, 60.5, 43.7, 14.2. HRMS (APCI+) *m/z*: $[M - OAllyl]^+$ calcd $C_{11}H_{13}O_2$ 177.0910; found 177.0913.

Ethyl 3-(allyloxy)-4-methylpentanoate (24c)

The reaction was conducted according to the procedure described for **24a** with known ethyl 3-hydroxy-4-methylpenanoate **23c**[34] (2.4 g, 15.0 mmol), *O*-allyl 2,2,2-trichloroacetimidate (4.5 mL, 29.6 mmol), and TfOH (0.1 mL, 1.13 mmol) in CH_2Cl_2 and pentanes (45 mL, 1 : 2) for 19 h. Purification *via* silica gel column chromatography (2% EtOAc/hexanes) afforded allyloxy **24c** (2.16 g 72%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.94–5.83 (m, 1H), 5.24 (dd, J = 17.2, 1.7 Hz, 1H), 5.12 (dd, J = 10.4, 1.6 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 4.04–4.00 (m, 2H), 3.63 (dt, J = 8.1, 4.7 Hz, 1H), 2.51–2.38 (m, 2H), 1.88 (pd, J = 6.9, 4.8 Hz, 1H), 1.26 (t, J = 7.1 Hz, 3H), 0.92 (dd, J = 6.9, 1.9 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 135.2, 116.4, 80.8, 71.3, 60.4, 37.0, 31.4, 18.0, 17.8, 14.2. HRMS (APCI+) *m/z*: $[M - OAllyl]^+$ calcd $C_{10}H_{13}O_2$ 165.0910; found 165.0911.

Ethyl 3-(3-hydroxypropoxy)butanoate (25a)

A two-neck round-bottom flask was charged with alkene **24a** (915 mg, 5.31 mmol) in THF (15 mL) and cooled to 0 °C, and 9-BBN (25 mL, 0.5 M in THF, 12.5 mmol) was added dropwise. The reaction was stirred for 30 min at 0 °C and then warmed to 23 °C and stirred for another 1.5 h. At the end of the reaction, a solution of $NaBO_3 \cdot 4\ H_2O$ (4.61 g, 30 mmol) in H_2O (100 mL) was prepared. The reaction mixture was transferred using a cannula into the water and stirred for 13 h. The solution was then diluted with EtOAc and the precipitates were filtered out. The aqueous layer was extracted with EtOAc (5×), and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure.

Purification *via* silica gel column chromatography (20–30% EtOAc/hexanes) afforded **25a** (665 mg, 66% yield) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (q, J = 7.1 Hz, 2H), 3.83 (dqd, J = 7.7, 6.2, 5.1 Hz, 1H), 3.71–3.64 (m, 3H), 3.51 (dt, J = 9.0, 6.1 Hz, 1H), 2.49 (dd, J = 15.1, 7.8 Hz, 1H), 2.35 (dd, J = 15.2, 5.1 Hz, 1H), 1.78–1.69 (m, 2H), 1.25–1.14 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 72.5, 67.3, 61.2, 60.4, 41.8, 32.1, 19.4, 14.0. HRMS (ESI+) *m/z*: $[M + Na]^+$ calcd $C_9H_{18}O_4Na$ 213.1103; found 213.1099.

Ethyl 3-(3-hydroxypropoxy)-3-phenylpropanoate (25b)

The reaction was conducted according to the procedure described for **24a** with alkene **24b** (1.24 g, 5.29 mmol) and 9-BBN (25 mL, 12.5 mmol) in THF (20 mL) and the mixture was stirred for 1.5 h; then $NaBO_3 \cdot 4\ H_2O$ (5.78 g, 37.6 mmol) in H_2O (250 mL) was added and stirred for 1 h. Purification *via* silica gel column chromatography (20–30% EtOAc/hexanes) afforded **25b** (878 mg, 66% yield) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.19 (m, 5H), 4.67 (dd, J = 9.5, 4.3 Hz, 1H), 4.08 (q, J = 7.1 Hz, 2H), 3.63 (ddd, J = 6.3, 5.7, 2.6 Hz, 2H), 3.48–3.33 (m, 2H), 2.86 (s, 1H), 2.72 (dd, J = 15.4, 9.5 Hz, 1H), 2.50 (dd, J = 15.4, 4.3 Hz, 1H), 1.70 (p, J = 5.9 Hz, 2H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 140.6, 128.5, 127.9, 126.3, 78.7, 67.3, 60.7, 60.5, 43.4, 32.1, 14.0. HRMS (ESI+) *m/z*: $[M + Na]^+$ calcd $C_{14}H_{20}O_4Na$ 275.1259; found 275.1260.

Ethyl 3-(3-hydroxypropoxy)-4-methylpentanoate (25c)

The reaction was conducted according to the procedure described for **24a** with alkene **24c** (2.16 g, 10.8 mmol) and 9-BBN (50 mL, 25 mmol) in THF (20 mL) and the mixture was stirred for 2.5 h; then $NaBO_3 \cdot 4\ H_2O$ (11.54 g, 75.0 mmol) in H_2O (250 mL) was added and stirred for 1.75 h. Purification *via* silica gel column chromatography (20–30% EtOAc/hexanes) afforded **25c** (2.36 g, 99% yield) as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.19–4.11 (m, 2H), 3.78–3.54 (m, 3H), 2.43 (dd, J = 6.3, 2.9 Hz, 2H), 1.90 (qd, J = 6.8, 3.4 Hz, 2H), 1.81–1.71 (m, 3H), 1.27 (dd, J = 8.3, 6.4 Hz, 6H), 0.91 (dd, J = 6.9, 2.8 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 81.6, 69.2, 61.6, 60.6, 36.6, 32.4, 31.1, 18.1, 17.6, 14.2. HRMS (ESI+) *m/z*: $[M + Na]^+$ calcd $C_{11}H_{122}O_4Na$ 241.1416; found 241.1411.

Ethyl 3-(but-3-en-1-yloxy)butanoate (26a)

To a flame dried round-bottom flask charged with alcohol **25a** (428.2 mg, 2.25 mmol) in CH_2Cl_2 (20 mL) at 0 °C, Dess–Martin periodinane (1.46 g, 3.45 mmol) was added; the reaction was stirred for 30 min, and then warmed to 23 °C and stirred for 15 min. The reaction was quenched with the addition of a 1 : 1 solution of 10% $Na_2S_2O_3$ and $NaHCO_3$ in water and extracted with CH_2Cl_2 (3×). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded ethyl 3-(3-oxopropoxy)butanoate (404.1 mg, 96% yield) as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.70 (s, 1H), 4.08 (q, J = 7.2 Hz, 2H), 3.83 (ddt, J = 21.8, 9.7, 6.0 Hz, 2H), 3.69 (dt, J = 9.7, 6.1 Hz, 1H), 2.56 (t, J = 5.8 Hz, 1H), 2.48 (dd, J = 15.2, 7.7 Hz, 1H), 2.31 (dd, J = 15.2, 5.4 Hz, 1H), 1.20 (t, J = 7.1 Hz, 3H), 1.15 (d, J = 6.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.3, 171.3, 72.6, 62.5, 60.4, 43.9, 41.9, 19.5, 14.2. HRMS (ESI+) *m/z*: $[M + Na]^+$ calcd $C_9H_{16}O_4Na$ 211.0946; found 211.0940.

The above aldehyde (384.5 mg, 2.04 mmol) was dissolved in THF (14 mL) and cooled to −78 °C. TMSMeMgCl (2.8 mL, 1.0 M in THF, 2.80 mmol) was added dropwise and the reaction was stirred for 45 min. Upon completion, the reaction was quenched with saturated NH_4Cl and extracted with EtOAc (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification *via* silica gel column chromatography (10–20% EtOAc/hexanes) afforded ethyl 3-(3-hydroxy-4-(trimethylsilyl)butoxy)butanoate (206.2 mg, 37% yield) as a colourless oil along with the recovery of the starting material (119.1 mg, 31% recovery). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.18–4.09 (m, 2H), 4.00–3.82 (m, 2H), 3.79–3.50 (m, 2H), 2.54 (ddd, J = 15.4, 7.7, 6.0 Hz, 1H), 2.38 (ddd, J = 15.0, 5.2, 2.7 Hz, 1H), 1.69 (tdd, J = 5.9, 4.8, 0.9 Hz, 1H), 1.26 (td, J = 7.1, 0.9 Hz, 3H), 1.21 (dd, J = 6.2, 3.5 Hz, 3H), 0.90 (ddd, J = 14.5, 8.1, 1.1 Hz, 1H), 0.76 (ddd, J = 14.5, 6.0, 1.1 Hz, 1H), 0.03 (d, J = 0.6 Hz, 9H). HRMS (ESI+) *m/z*: $[M + Na]^+$ calcd $C_{13}H_{28}O_4SiNa$ 299.1655; found 299.1642.

The above alcohol (40.7 mg, 0.147 mmol) was dissolved in CH_2Cl_2 (5 mL) and cooled to −78 °C; then $BF_3 \cdot OEt_2$ (32 µL, 0.262 mmol) was added dropwise. The reaction mixture was stirred for 2 h, warmed to 0 °C and stirred for another 4.5 h. The reaction was quenched with H_2O and extracted with CH_2Cl_2 (3×). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified *via* silica gel column chromatography (10% EtOAc/hexanes) to give homoallyloxy **26a** (23.6 mg, 86% yield, 31% overall yield) as a colourless oil.[12] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 5.06 (dq, J = 17.2, 1.7 Hz, 1H), 5.00 (ddt, J = 10.2, 2.1, 1.2 Hz, 1H), 4.13 (q, J = 7.2 Hz, 2H), 3.86 (dp, J = 7.4, 6.1 Hz, 1H), 3.54 (dt, J = 9.1, 6.7 Hz, 1H), 3.43 (dt, J = 9.2, 6.8 Hz, 1H), 2.56 (dd, J = 14.9, 7.4 Hz, 1H), 2.34 (dd, J = 15.0, 5.8 Hz, 1H), 2.28 (qt, J = 6.9, 1.5 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H), 1.19 (d, J = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 135.2, 116.1, 72.2, 68.1, 60.2, 42.0, 34.3, 19.7, 14.1.

Ethyl 3-(but-3-en-1-yloxy)-3-phenylpropanoate (26b)

The reaction was conducted according to the procedure described for **26a** with alcohol **25b** (6.66 g, 26.4 mmol) and Dess–Martin periodinane (15.72 g, 37.1 mmol) in CH_2Cl_2 (250 mL) for 1.5 h. The product was purified *via* silica gel column chromatography (20% EtOAc/hexanes) to give ethyl 3-(3-oxopropoxy)-3-phenylpropanoate (45.2 mg, 76%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (td, J = 2.0, 0.5 Hz, 1H), 7.39–7.27 (m, 5H), 4.76 (dd, J = 9.4, 4.5 Hz, 1H), 4.13 (qd, J = 7.1, 1.0 Hz, 2H), 3.72–3.61 (m, 2H), 2.77 (dd, J = 15.5, 9.4 Hz, 1H), 2.62–2.51 (m, 3H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 170.7, 140.4, 128.6, 128.1, 126.4, 78.8, 62.8, 60.5, 43.5, 43.4, 14.1. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{14}H_{18}O_4Na$ 273.1097; found 273.1104.

The above aldehyde (5.21 g, 20.8 mmol) was dissolved in THF (200 mL) and cooled to −78 °C. TMSMeMgCl (42 mL, 1.0 M in THF, 42 mmol) was added dropwise and the reaction mixture was stirred for 30 min. Upon completion, the reaction was quenched with saturated NH_4Cl and extracted with EtOAc (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification *via* silica gel column chromatography (10–20% EtOAc/hexanes) afforded ethyl 3-(3-hydroxy-4-(trimethylsilyl)butoxy)-3-phenylpropanoate (2.2 g, 31% yield) as a colourless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.39–7.28 (m, 5H), 4.72 (dt, *J* = 9.6, 3.8 Hz, 1H), 4.19–4.11 (m, 2H), 4.00–3.91 (m, 1H), 3.57–3.44 (m, 2H), 2.80 (ddd, *J* = 15.6, 9.6, 1.5 Hz, 1H), 2.61–2.52 (m, 1H), 1.75–1.61 (m, 2H), 1.25 (td, *J* = 7.2, 1.9 Hz, 3H), 0.94–0.71 (m, 2H), 0.03 (d, *J* = 1.7 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 171.0, 140.7, 140.5, 128.7, 128.2, 128.1, 126.6, 126.5, 79.1, 69.9, 68.6, 68.4, 67.6, 60.8, 60.7, 43.5, 43.4, 39.7, 39.6, 26.4, 26.2, 14.2, 14.2, −0.7. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{18}H_{30}O_4SiNa$ 361.1811; found 361.1804.

The above alcohol (2.2 g, 6.48 mmol) was dissolved in CH_2Cl_2 (50 mL) and cooled to −78 °C; then $BF_3 \cdot OEt_2$ (0.9 mL, 7.36 mmol) was added dropwise and the reaction mixture was stirred for 1.5 h. The reaction was quenched with H_2O and extracted with CH_2Cl_2 (3×). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified *via* silica gel column chromatography (10% EtOAc/hexanes) to give homoallyloxy **26b** (1.18 g, 73% yield, 17% overall yield) as a colourless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.25 (m, 5H), 5.77 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.06–4.95 (m, 2H), 4.75 (dd, *J* = 9.2, 4.7 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.37 (ddt, *J* = 27.7, 9.3, 6.7 Hz, 2H), 2.80 (dd, *J* = 15.2, 9.2 Hz, 1H), 2.56 (dd, *J* = 15.2, 4.7 Hz, 1H), 2.35–2.23 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 141.2, 135.3, 128.5, 127.9, 126.6, 116.2, 78.6, 68.5, 60.5, 43.8, 34.1, 14.2. HRMS (APCI+) *m*/*z*: $[M + Na]^+$ calcd $C_{15}H_{20}O_3Na$ 171.1305; found 171.1335.

Ethyl 3-(but-3-en-1-yloxy)-4-methylpentanoate (26c)

The reaction was conducted according to the procedure described for **26a** with alcohol **25c** (545 mg, 2.5 mmol) and Dess–Martin periodinane (1.58 g, 3.73 mmol) in CH_2Cl_2 (25 mL) for 1.5 h. The product was purified *via* silica gel column chromatography (20% EtOAc/hexanes) to give ethyl 4-methyl-3-(3-oxopropoxy)pentanoate (481 mg, 89%) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 9.75 (t, *J* = 2.0 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.89–3.77 (m, 2H), 3.61 (dt, *J* = 7.8, 4.9 Hz, 1H), 2.62–2.56 (m, 2H), 2.40 (dd, *J* = 6.4, 4.0 Hz, 2H), 1.87 (pd, *J* = 6.9, 5.0 Hz, 1H), 1.25 (d, *J* = 7.1 Hz, 3H), 0.89 (dd, *J* = 6.9, 3.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.5, 172.2, 81.3, 63.9, 60.4, 43.9, 36.5, 31.0, 17.9, 17.5, 14.1. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{11}H_{20}O_4Na$ 239.1259; found 239.1250.

The above aldehyde (831 mg, 3.84 mmol) was dissolved in THF (200 mL) and cooled to −78 °C. TMSMeMgCl (7.7 mL, 1.0 M in THF, 7.7 mmol) was added dropwise and the reaction mixture was stirred for 25 min. Upon completion, the reaction was quenched with saturated NH_4Cl and extracted with EtOAc (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification *via* silica gel column chromatography (10–20% EtOAc/hexanes) afforded ethyl 3-(3-hydroxy-4-(trimethylsilyl)butoxy)-4-methylpentanoate (181 mg, 15% yield) as a colourless oil along with the recovery of the starting material (91.5 mg, 11% recovery). ^1H NMR (500 MHz, $CDCl_3$) δ 4.15 (qd, *J* = 7.2, 2.2 Hz, 2H), 3.99–3.91 (m, 1H), 3.74–3.60 (m, 2H), 3.57 (dtd, *J* = 8.0, 4.7, 1.6 Hz, 1H), 2.93 (s, 1H), 2.48–2.37 (m, 2H), 1.89 (dqd, *J* = 11.9, 6.9, 5.1 Hz, 1H), 1.74–1.56 (m, 2H), 1.26 (td, *J* = 7.1, 2.5 Hz, 3H), 0.90 (ddd, *J* = 6.9, 3.0, 1.4 Hz, 7H), 0.03 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 172.4, 81.7, 81.6, 70.0, 69.4, 68.9, 68.6, 60.6, 40.0, 39.9, 36.6, 36.5, 31.1, 30.9, 26.4, 26.2, 18.1, 18.0, 17.6, 14.2, −0.7, −0.7. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{15}H_{32}O_4SiNa$ 327.1968; found 327.1956.

The above alcohol (48.3 mg, 0.159 mmol) was dissolved in CH_2Cl_2 (5 mL) and cooled to −78 °C; then $BF_3 \cdot OEt_2$ (30 μL, 0.245 mmol) was added dropwise and the reaction mixture was stirred for 3 h. The reaction was quenched with H_2O and extracted with CH_2Cl_2 (3×). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified *via* silica gel column chromatography (10% EtOAc/hexanes) to give homoallyloxy **26c** (19.8 mg, 58% yield, 8% overall yield) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.06 (dq, *J* = 17.3, 1.9 Hz, 1H), 5.00 (ddt, *J* = 10.3, 2.2, 1.2 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.56 (dt, *J* = 8.0, 4.9 Hz, 1H), 3.51 (t, *J* = 6.8 Hz, 2H), 2.47–2.35 (m, 2H), 2.27 (qt, *J* = 6.8, 1.4 Hz, 2H), 1.86 (heptd, *J* = 6.8, 5.0 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.90 (dd, *J* = 6.8, 4.1 Hz, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 135.4, 116.0, 81.1, 69.6, 60.3, 36.8, 34.5, 31.3, 18.0, 17.6, 14.1. HRMS (ESI+) *m*/*z*: $[M - OCH_2CH_2CHCH_2]^+$ calcd $C_8H_{15}O_2$ 143.1067; found 143.1063.

3-(But-3-en-1-yloxy)-1-(furan-2-yl)butan-1-ol (27a)

To a round bottom flask charged with ester **26a** (188 mg, 1.01 mmol) in CH_2Cl_2 (10 mL) at −78 °C, DIBAL (1.1 mL, 1.0 M, 1.10 mmol) was added dropwise and stirred for 30 min. The reaction was quenched with MeOH (0.12 mL, 2.96 mmol) and a saturated solution of Rochelle's salt in water (0.5 mL) was added; then the reaction was slowly warmed to 23 °C. The resulting slurry was filtered over a layer of Na_2SO_4 and a layer of Celite, and the clear solution was then concentrated under reduced pressure.

A solution of 2-lithiofuran was prepared by charging a dry round bottom flask with furan (240 μL, 3.30 mmol) in THF (4 mL) and cooled to 0 °C. *n*-BuLi (2 mL, 1.5 M in hexanes, 3 mmol) was added dropwise and the reaction mixture was stirred for 30 min and then cooled to −78 °C. The crude aldehyde from the above reaction was dissolved in THF (6 mL) and cannulated into the solution of 2-lithiofuran and continued to stir at −78 °C for 15 min. The reaction mixture was stirred for 15 min, quenched with saturated NH_4Cl, and warmed to 23 °C. The solution was diluted with EtOAc and the organic layers were separated. The aqueous layer was extracted with EtOAc (3×); the combined organic layers were washed with ice and brine sequentially, dried over Na_2SO_4, and concentrated under reduced pressure. Purification *via* silica gel column chromatography (14% EtOAc/hexanes) afforded **27a** (11.5 mg, 52% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (s, 1H), 6.30 (dd, J = 3.2, 1.9 Hz, 1H), 6.22 (d, J = 3.2 Hz, 1H), 5.81 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H), 5.15–5.03 (m, 2H), 4.90 (dd, J = 9.5, 3.2 Hz, 1H), 3.95 (s, 1H), 3.76–3.64 (m, 2H), 3.37 (dt, J = 9.0, 6.7 Hz, 1H), 2.37–2.28 (m, 2H), 2.18–1.96 (m, 1H), 1.89 (dt, J = 14.5, 3.2 Hz, 1H), 1.19 (d, J = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 141.5, 134.9, 116.9, 110.0, 105.3, 76.0, 67.7, 67.4, 42.4, 34.4, 19.5. HRMS (APCI+) m/z: $[M - OH]^+$ calcd $C_{12}H_{17}O_2$ 193.1223; found 193.1224.

3-(But-3-en-1-yloxy)-1-(furan-2-yl)-3-phenylpropan-1-ol (27b)

The reaction was conducted according to the procedure described for **27a** with ester **26b** (64.3 mg, 0.26 mmol) and DIBAL (0.27 mL, 1.0 M, 0.27 mmol) in CH_2Cl_2 (2.6 mL). 2-Lithiofuran was prepared from furan (65 μL, 0.895 mmol) and *n*-BuLi (0.5 mL, 1.6 M in hexanes, 0.8 mmol) in THF (1.6 mL). The crude aldehyde obtained from DIBAL reducion, was cannulated over in THF (1 mL) and stirred for 30 min. Purification *via* silica gel column chromatography (14% EtOAc/hexanes) afforded **27b** (16.0 mg, 23% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.25 (m, 7H), 6.36–6.21 (m, 2H), 5.81 (ddq, J = 17.0, 10.2, 6.6 Hz, 1H), 5.15–5.04 (m, 2H), 4.97 (ddd, J = 8.9, 7.0, 3.0 Hz, 1H), 4.52 (ddd, J = 21.1, 9.8, 3.5 Hz, 1H), 3.96 (s, 1H), 3.43 (dq, J = 9.2, 6.2 Hz, 1H), 3.32 (ddt, J = 22.6, 9.3, 6.6 Hz, 1H), 2.38–2.27 (m, 3H), 2.29–2.14 (m, 1H), 2.07 (dt, J = 14.7, 3.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 156.3, 141.8, 141.7, 141.4, 135.3, 135.0, 128.6, 128.6, 128.0, 127.7, 126.4, 126.4, 117.1, 116.8, 110.2, 110.1, 105.8, 105.5, 82.8, 79.8, 68.2, 68.0, 67.8, 65.9, 44.0, 43.1, 34.3, 34.3. LRMS-ESI (m/z) $[M + Na]^+$ 295.1.

3-(But-3-en-1-yloxy)-1-(furan-2-yl)-4-methylpentan-1-ol (27c)

The reaction was conducted according to the procedure described for **27a** with ester **26c** (73.9 mg, 0.35 mmol) and DIBAL (0.5 mL, 1.0 M, 0.5 mmol) in CH_2Cl_2 (3.5 mL). 2-Lithiofuran was prepared from furan (85 μL, 1.17 mmol) and *n*-BuLi (0.65 mL, 1.6 M in hexanes, 1.04 mmol) in THF (2.5 mL). The crude aldehyde obtained from DIBAL reduction, was cannulated over in THF (1 mL) and stirred for 15 min. Purification *via* silica gel column chromatography (14% EtOAc/hexanes) afforded **27c** (34.0 mg, 41% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.34 (m, 1H), 6.32 (dd, J = 3.3, 1.8 Hz, 1H), 6.24 (d, J = 3.2 Hz, 1H), 5.82 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H), 5.16–5.05 (m, 2H), 4.89 (dd, J = 9.0, 3.7 Hz, 1H), 3.94 (s, 1H), 3.68 (dt, J = 9.0, 6.4 Hz, 1H), 3.46–3.37 (m, 2H), 2.39–2.29 (m, 2H), 2.06 (pd, J = 6.9, 4.1 Hz, 1H), 1.98–1.84 (m, 2H), 0.88 (dd, J = 6.9, 6.9 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.8, 141.7, 135.1, 117.1, 110.1, 105.4, 84.8, 68.3, 68.1, 34.7, 29.2, 18.5, 15.8. HRMS (ESI+) m/z: $[M - OH]^+$ calcd $C_{14}H_{21}O_2$ 221.1536; found 221.1536.

2-Methyloctahydro-1*H*-3a,7-epoxyazulen-4-ol (28)

Cycloadduct **10a** (16 mg, 98.1 μmol) was dissolved in EtOAc (3 mL), and Rh/AlO_3 (4.5 mg, 5% Rh) was added. The flask was flushed with argon and hydrogen sequentially and then stirred under a hydrogen-filled balloon for 1 h. The reaction was flushed with argon before filtering the solids out over Celite to give the alcohol as a mixture of diastereomers. The mixture of alcohols was dissolved in CH_2Cl_2 and DMP (179 mg, 0.42 mmol) and $NaHCO_3$ (70.3 mg, 0.84 mmol) were added in portions. The reaction mixture was stirred for 4 h and then quenched with aqueous $NaHCO_3$ and 10% $Na_2S_2O_3$. The organic layer was separated, and the aqueous layer was washed with CH_2Cl_2 (3×). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude ketone was dissolved in dry MeOH (3 mL) and cooled to −78 °C, and $NaBH_4$ (7.2 mg, 0.19 mmol) was added. The reaction mixture was stirred for 15 min and then quenched with aq. sat. NH_4Cl. The reaction was diluted with EtOAc, the organic layer was separated, and the aqueous layer was washed with EtOAc (5×). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Purification *via* silica gel column chromatography (15% EtOAc/hexanes) gave alcohol **28** (6.6 mg, 37% in 3-step) as a clear oil. ^{1}H NMR (800 MHz, DMSO) δ 4.66 (d, J = 5.7 Hz, 1H), 4.29 (dd, J = 7.3, 3.8 Hz, 1H), 3.43–3.34 (m, 1H), 2.42 (ddt, J = 15.1, 10.9, 5.7 Hz, 1H), 2.11 (ddd, J = 13.0, 8.3, 1.6 Hz, 1H), 1.93–1.86 (m, 2H), 1.70 (dt, J = 12.3, 7.5 Hz, 2H), 1.60 (ddd, J = 12.1, 7.2, 4.3 Hz, 1H), 1.57–1.51 (m, 1H), 1.33–1.26 (m, 2H), 1.05 (dd, J = 13.1, 10.2 Hz, 1H), 0.93 (d, J = 6.2 Hz, 3H), 0.92–0.87 (m, 1H). ^{13}C NMR (201 MHz, DMSO) δ 94.9, 77.1, 69.2, 43.4, 41.8, 41.7, 37.4, 35.9, 30.7, 27.1, 19.9. HRMS (APCI+) m/z: $[M - OH]^+$ calcd $C_{11}H_{17}O$ 165.1274; found 165.1278.

6-(2-Methylpent-4-en-1-yl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9a)

To a round bottom flask charged with furanyl alcohol **14a** (65.5 mg, 0.36 mmol) in a mixture of THF and water (4 mL, 4 : 1) at 0 °C, KBr (10 mg, 0.08 mmol), $NaHCO_3$ (15.6 mg, 0.18 mmol), and Oxone (364 mg, 1.19 mmol) were added at the same time and stirred for 30 min. Upon completion of the reaction, the solution was diluted with EtOAc and water, the solids were filtered out, and the organic layers were separated. The aqueous layer was extracted with EtOAc (3×); the combined organic layers were washed with ice and brine sequentially, dried over Na_2SO_4, and concentrated under reduced pressure.

To crude lactol in CH_2Cl_2 (4 mL) at 0 °C, pyridine (60 μL, 0.745 mmol) and AcCl (40 μL, 0.71 mmol) were added sequentially and stirred for 30 min. Upon completion, the reaction was quenched with saturated $NaHCO_3$ solution. The organic layer was separated, and the aqueous layer was washed with CH_2Cl_2 (3×). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Purification *via* silica gel column chromatography (16% EtOAc/hexanes) afforded **9a** (46 mg, 53% yield) as a yellow oil. ^{1}H NMR

(400 MHz, $CDCl_3$) δ 6.90–6.79 (m, 1H), 6.55–6.44 (m, 1H), 6.24–6.14 (m, 1H), 5.83–5.67 (m, 1H), 5.06–4.94 (m, 2H), 4.57–4.26 (m, 1H), 2.19–1.45 (m, 6H), 0.95–0.84 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 195.8, 195.7, 195.6, 169.4, 169.2, 142.5, 142.5, 141.3, 141.1, 136.8, 136.7, 136.5, 136.4, 128.5, 128.2, 128.1, 116.3, 116.2, 116.1, 87.4, 86.9, 77.7, 77.5, 77.1, 74.2, 73.8, 41.9, 41.7, 40.1, 39.9, 39.3, 39.2, 35.6, 35.5, 28.8, 28.7, 28.5, 28.3, 20.9, 20.8, 20.0, 19.9, 18.2, 18.1. HRMS (APCI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{11}H_{15}O_2$ 179.1067; found 179.1073.

5-Oxo-6-(2-phenylpent-4-en-1-yl)-5,6-dihydro-2*H*-pyran-2-yl acetate (9b)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **14b** (88.7 mg, 0.366 mmol), KBr (12.2 mg, 0.10 mmol), $NaHCO_3$ (16.6 mg, 0.2 mmol), and Oxone (325 mg, 1.06 mmol) in THF and water (4 : 1, 5 mL) for 30 min. The crude lactol was protected by treatment with pyridine (60 μL, 0.745 mmol) and AcCl (40 μL, 0.712 mmol) in CH_2Cl_2 (5 mL) for 30 min. Purification *via* silica gel column chromatography (16% EtOAc/hexanes) afforded **9b** (73.5 mg, 67% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.13 (m, 5H), 6.84–6.73 (m, 1H), 6.51–6.43 (m, 1H), 6.21–6.06 (m, 1H), 5.72–5.57 (m, 1H), 5.03–4.90 (m, 2H), 4.44–3.76 (m, 1H), 3.08–2.88 (m, 1H), 2.50–1.90 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 195.7, 195.6, 169.5, 169.4, 169.4, 169.2, 144.2, 144.0, 143.3, 142.8, 142.5, 141.3, 140.9, 136.5, 136.5, 136.1, 128.8, 128.7, 128.7, 128.5, 128.4, 128.3, 128.0, 128.0, 127.8, 126.7, 126.5, 126.4, 126.4, 116.6, 116.4, 116.3, 88.1, 87.5, 86.9, 86.4, 73.9, 73.2, 60.4, 41.5, 41.3, 41.3, 41.1, 40.8, 40.8, 40.2, 40.1, 39.2, 38.3, 35.9, 35.0, 21.1, 21.0, 20.8, 14.2. HRMS (APCI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{16}H_{17}O_2$ 241.1223; found 241.1232.

6-(2-Isopropylpent-4-en-1-yl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9c)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **14c** (82.4 mg, 0.396 mmol), KBr (12.3 mg, 0.103 mmol), $NaHCO_3$ (17 mg, 0.198 mmol) and Oxone (365 mg, 1.19 mmol) in THF and water (4 : 1, 5 mL) for 20 min. The crude lactol was protected by treatment with pyridine (65 μL, 0.807 mmol) and AcCl (45 μL, 0.801 mmol) in CH_2Cl_2 (5 mL) for 20 min. Purification *via* silica gel column chromatography (16% EtOAc/hexanes) afforded **9c** (63.0 mg, 60% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 6.84 (ddd, *J* = 10.3, 4.9, 3.2 Hz, 1H), 6.54–6.43 (m, 1H), 6.25–6.13 (m, 1H), 5.84–5.64 (m, 1H), 5.07–4.91 (m, 2H), 4.57–4.24 (m, 1H), 2.19–1.49 (m, 8H), 0.96–0.75 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 169.3, 142.7, 142.6, 141.2, 141.2, 137.8, 137.7, 137.5, 128.5, 128.3, 128.2, 115.8, 115.7, 115.6, 87.8, 87.6, 87.0, 77.8, 77.6, 74.3, 74.0, 38.9, 38.4, 38.3, 35.0, 34.7, 34.5, 33.8, 33.6, 30.0, 29.8, 29.7, 28.4, 27.9, 21.0, 20.8, 19.6, 19.5, 18.3, 18.1, 17.8, 17.4. HRMS (APCI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{13}H_{19}O_2$ 207.1385; found 207.1390.

6-(2-Methylhex-5-en-1-yl)-5-oxotetrahydro-2*H*-pyran-2-yl acetate (9d)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **18** (52.4 mg, 0.24 mmol), KBr (6.2 mg, 0.05 mmol), $NaHCO_3$ (13.7 mg, 0.16 mmol) and Oxone (225.6 mg, 0.75 mmol) in THF and water (4 : 1, 5 mL) for 45 min. The crude lactol was protected by treatment with pyridine (40 μL, 0.49 mmol) and AcCl (25 μL, 0.44 mmol) in CH_2Cl_2 (5 mL) for 18.5 h. Purification *via* silica gel column chromatography (5–10% EtOAc/hexanes) afforded **9d** (36.2 mg, 59% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 6.85 (dtd, *J* = 10.9, 6.9, 3.8 Hz, 1H), 6.51 (dd, *J* = 23.7, 2.4 Hz, 1H), 6.24–6.16 (m, 1H), 5.79 (ddt, *J* = 13.4, 10.2, 6.7 Hz, 1H), 5.05–4.87 (m, 2H), 4.56–4.12 (m, 1H), 2.19–1.91 (m, 5H), 1.84–1.12 (m, 4H), 0.90 (dd, *J* = 8.6, 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 195.8, 169.4, 142.5, 141.2, 141.1, 138.9, 128.5, 114.2, 87.0, 86.9, 74.1, 73.9, 36.6, 36.0, 35.9, 34.8, 31.1, 30.9, 28.5, 28.0, 20.8, 19.9, 18.3. HRMS (APCI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{12}H_{17}O_2^+$ 193.1223; found 193.1222.

6-(2-(Allyloxy)propyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9e)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **22a** (26.3 mg, 0.134 mmol), KBr (6.2 mg, 0.05 mmol), $NaHCO_3$ (5.5 mg, 0.0655 mmol) and Oxone (127.8 mg, 0.42 mmol) in THF and water (4 : 1, 2 mL) for 15 min. The crude lactol was protected by treatment with pyridine (20 μL, 0.25 mmol) and AcCl (20 μL, 0.28 mmol) in CH_2Cl_2 (2 mL) for 30 min. Purification *via* silica gel column chromatography (25% EtOAc/hexanes) afforded **9e** (25 mg, 44% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 6.88–6.80 (m, 1H), 6.57–6.44 (m, 1H), 6.21 (ddd, *J* = 10.3, 4.7, 2.3 Hz, 1H), 5.99–5.76 (m, 1H), 5.30–5.06 (m, 2H), 4.79–4.34 (m, 1H), 4.13–3.61 (m, 3H), 2.12 (dd, *J* = 10.1, 3.2 Hz, 4H), 1.17 (dd, *J* = 13.0, 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 169.5, 143.0, 142.8, 141.0, 140.3, 135.2, 135.1, 135.0, 128.9, 128.7, 116.5, 116.3, 116.2, 116.0, 87.7, 86.8, 73.2, 72.4, 71.3, 70.9, 69.9, 69.6, 69.3, 69.3, 39.4, 39.1, 36.7, 21.0, 20.8, 19.8, 19.2. HRMS (APCI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{11}H_{15}O_3$ 195.1016; found 195.1018.

6-(2-(Allyloxy)-2-phenylethyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9f)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **22b** (110 mg, 0.42 mmol), KBr (13.6 mg, 0.11 mmol), $NaHCO_3$ (19 mg, 0.22 mmol) and Oxone (404 mg, 1.32 mmol) in THF and water (4 : 1, 5 mL) for 20 min. The crude lactol was protected by treatment with pyridine (70 μL, 0.87 mmol) and AcCl (50 μL, 0.89 mmol) in CH_2Cl_2 (5 mL) for 1 h. Purification *via* silica gel column chromatography (16% EtOAc/hexanes) afforded **9f** (97 mg, 72% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.39–7.23 (m, 6H), 6.31 (ddt, *J* = 8.9, 3.1, 1.5 Hz, 1H), 6.26–6.20 (m, 1H), 5.97–5.92 (m, 1H), 5.82 (dddd, *J* = 16.6, 10.2, 8.6, 5.0 Hz, 1H), 5.25–5.10 (m, 2H), 4.51–3.53 (m, 4H), 2.65–2.17 (m, 2H), 2.06–1.99 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.9, 169.7, 143.1, 143.0, 141.9, 140.9, 140.5, 134.9, 134.7, 134.4, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 128.0, 127.9, 127.2, 127.1, 126.6, 126.5, 126.3, 116.7, 116.6, 116.3, 88.3, 87.9, 86.7, 73.2, 70.4, 69.7, 69.6, 69.5, 41.2, 40.3, 37.8, 21.2, 21.0. HRMS (ESI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{16}H_{17}O_3$ 257.1178; found 257.1166.

6-(2-(Allyloxy)-3-methylbutyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9g)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **22c** (231.8 mg, 1.03 mmol), KBr (27 mg, 0.22 mmol), $NaHCO_3$ (42 mg, 0.506 mmol) and Oxone (983 mg, 3.20 mmol) in THF and water (4 : 1, 10 mL) for 25 min. The crude lactol was protected by treatment with pyridine (160 µL, 1.99 mmol) and AcCl (112 µL, 1.99 mmol) in CH_2Cl_2 (10 mL) for 30 min. Purification *via* silica gel column chromatography (25% EtOAc/hexanes) afforded **9g** (25.1 mg, 44% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94–6.83 (m, 1H), 6.60–6.52 (m, 1H), 6.30–6.23 (m, 1H), 6.04–5.81 (m, 1H), 5.35–5.10 (m, 2H), 4.80–4.39 (m, 1H), 4.18–3.88 (m, 2H), 3.50–3.38 (m, 1H), 2.26–1.85 (m, 6H), 0.95 (ddd, *J* = 6.8, 4.4, 2.3 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 195.5, 169.6, 169.2, 143.1, 143.0, 141.2, 140.2, 135.4, 135.3, 135.2, 129.0, 128.9, 128.8, 116.3, 116.2, 116.1, 115.9, 88.3, 88.0, 87.0, 80.3, 79.9, 78.9, 78.8, 73.6, 72.8, 71.8, 71.4, 70.9, 70.6, 33.7, 33.6, 31.2, 31.0, 30.9, 30.7, 30.6, 30.4, 21.1, 21.0, 18.4, 18.3, 18.0, 17.7, 17.5, 17.4, 17.1. HRMS (APCI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{13}H_{19}O_3$ 223.1329; found 223.1330.

6-(2-(Allyloxy)-3,3-dimethylbutyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9h)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **22d** (286 mg, 1.2 mmol), KBr (31 mg, 0.26 mmol), $NaHCO_3$ (52 mg, 0.62 mmol) and Oxone (1.12 g, 3.64 mmol) in THF and water (4 : 1, 12 mL) for 25 min. The crude lactol was protected by treatment with pyridine (0.2 mL, 2.48 mmol) and AcCl (135 µL, 2.4 mmol) in CH_2Cl_2 (12 mL) for 30 min. Purification *via* silica gel column chromatography (16% EtOAc/hexanes) afforded **9h** (319 mg, 90% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (dddd, *J* = 23.7, 10.1, 3.2, 1.8 Hz, 1H), 6.62–6.55 (m, 1H), 6.32–6.22 (m, 1H), 6.04–5.82 (m, 1H), 5.39–5.21 (m, 1H), 5.20–5.08 (m, 1H), 4.77–4.37 (m, 1H), 4.25–4.02 (m, 3H), 3.34–3.16 (m, 1H), 2.22–2.13 (m, 4H), 2.11–1.91 (m, 2H), 0.98–0.94 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 195.7, 169.6, 169.2, 143.1, 141.1, 140.3, 135.3, 135.1, 129.0, 128.8, 128.7, 115.8, 115.7, 88.3, 87.9, 87.1, 87.1, 84.3, 83.9, 82.9, 74.7, 74.5, 74.2, 73.7, 73.3, 36.1, 35.8, 34.6, 33.5, 32.0, 31.3, 26.3, 26.3, 26.2, 26.2, 21.1, 21.0, 14.2. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{16}H_{24}O_5Na$ 319.1521; found 319.1509.

6-(2-(Allyloxy)-3-phenylpropyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9i)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **22e** (29.5 mg, 0.11 mmol), KBr (29 mg, 0.24 mmol), $NaHCO_3$ (46 mg, 0.54 mmol) and Oxone (101 mg, 0.33 mmol) in THF and water (4 : 1, 10 mL) for 15 min. The crude lactol was protected by treatment with pyridine (20 µL, 0.25 mmol) and AcCl (15 µL, 0.27 mmol) in CH_2Cl_2 (10 mL) for 30 min. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded **9i** (21 mg, 58% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.25 (m, 6H), 7.21 (td, *J* = 8.8, 2.7 Hz, 5H), 6.90–6.78 (m, 1H), 6.55–6.47 (m, 1H), 6.25–6.16 (m, 2H), 5.86–5.70 (m, 1H), 5.22–5.05 (m, 2H), 4.73–4.35 (m, 1H), 4.17–3.34 (m, 5H), 2.97–2.68 (m, 3H), 2.21–1.90 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.3, 169.1, 143.1, 140.3, 134.8, 129.6, 129.5, 129.0, 128.3, 126.2, 116.6, 116.5, 88.0, 86.9, 73.1, 70.5, 70.4, 40.8, 40.7, 36.8, 34.5, 21.0. HRMS (ESI+) *m*/*z*: $[M + Na]^+$ calcd $C_{19}H_{22}O_5Na$ 353.1359; found 353.1354.

6-(2-(But-3-en-1-yloxy)propyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9j)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **27a** (96 mg, 0.46 mmol), KBr (11.0 mg, 0.09 mmol), $NaHCO_3$ (21.6 mg, 0.26 mmol) and Oxone (425.2 mg, 1.38 mmol) in THF and water (4 : 1, 5 mL) for 40 min. The crude lactol was protected by treatment with pyridine (75 µL, 0.93 mmol) and AcCl (50 µL, 0.89 mmol) in CH_2Cl_2 (5 mL) for 30 min. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded **9j** (94 mg, 77% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (ddt, *J* = 10.1, 5.4, 3.6 Hz, 1H), 6.51–6.42 (m, 1H), 6.16 (dd, *J* = 10.2, 7.5 Hz, 1H), 5.73 (dddd, *J* = 23.6, 16.9, 10.4, 6.8 Hz, 1H), 5.07–4.90 (m, 2H), 4.71–4.29 (m, 1H), 4.06 (q, *J* = 7.1 Hz, 1H), 3.71–3.51 (m, 1H), 3.46 (ddt, *J* = 15.7, 9.1, 6.8 Hz, 1H), 3.31 (ddt, *J* = 34.7, 9.3, 6.9 Hz, 1H), 2.30–1.86 (m, 9H), 1.23–1.17 (m, 1H), 1.14–1.08 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.7, 195.6, 195.3, 195.2, 171.0, 169.5, 169.5, 169.1, 169.0, 143.1, 142.9, 141.2, 140.5, 135.6, 135.4, 135.3, 128.9, 128.8, 128.6, 116.3, 116.2, 116.1, 88.1, 87.8, 87.0, 86.9, 73.2, 72.6, 71.7, 71.4, 70.5, 70.4, 68.1, 67.8, 67.8, 60.3, 39.6, 39.3, 36.9, 36.7, 34.6, 34.5, 34.4, 21.0, 21.0, 20.9, 20.8, 19.9, 19.9, 19.3, 19.3, 14.2. HRMS (ESI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{12}H_{17}O_3$ 209.1172; found 209.1150.

6-(2-(But-3-en-1-yloxy)-2-phenylethyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9k)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **27b** (268 mg, 0.98 mmol), KBr (23.4 mg, 0.196 mmol), $NaHCO_3$ (42.5 mg, 0.51 mmol) and Oxone (926 mg, 3.02 mmol) in THF and water (4 : 1, 10 mL) for 30 min. The crude lactol was protected by treatment with pyridine (160 µL, 1.99 mmol) and AcCl (110 µL, 1.96 mmol) in CH_2Cl_2 (10 mL) for 30 min. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded **9k** (116 mg, 36% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H), 6.91–6.78 (m, 1H), 6.61–6.47 (m, 1H), 6.26–6.18 (m, 1H), 5.87–5.67 (m, 1H), 5.10–4.94 (m, 2H), 4.55–4.43 (m, 1H), 4.26–4.02 (m, 1H), 3.45–3.22 (m, 2H), 2.52–2.07 (m, 10H). ^{13}C NMR (125 MHz,

$CDCl_3$) δ 195.5, 194.9, 169.6, 169.3, 143.1, 142.9, 141.2, 141.1, 140.6, 135.4, 135.3, 135.3, 128.9, 128.8, 128.6, 128.5, 128.5, 127.9, 127.9, 127.7, 127.1, 127.0, 126.5, 116.3, 116.2, 87.9, 87.1, 86.7, 78.5, 78.2, 76.5, 73.2, 72.6, 68.4, 68.3, 68.2, 41.3, 40.4, 37.9, 34.4, 34.3, 34.3, 30.9, 21.1, 21.0. HRMS (ESI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{17}H_{19}O_3$ 271.1329; found 271.1330.

6-(2-(But-3-en-1-yloxy)-3-methylbutyl)-5-oxo-5,6-dihydro-2*H*-pyran-2-yl acetate (9l)

The reaction was conducted according to the procedure described for **9a** with furanyl alcohol **27c** (34 mg, 0.14 mmol), KBr (3.9 mg, 0.03 mmol), $NaHCO_3$ (6.8 mg, 0.81 mmol) and Oxone (133.3 mg, 0.434 mmol) in THF and water (4 : 1, 5 mL) for 45 min. The crude lactol was protected by treatment with pyridine (25 μL, 0.310 mmol) and AcCl (16 μL, 0.28 mmol) in CH_2Cl_2 (2 mL) for 1.5 h. Purification *via* silica gel column chromatography (20% EtOAc/hexanes) afforded **9l** (19.5 mg, 46% yield) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 6.89–6.79 (m, 1H), 6.55–6.47 (m, 1H), 6.26–6.17 (m, 1H), 5.81 (tddt, *J* = 17.1, 13.5, 10.3, 6.7 Hz, 1H), 5.12–4.94 (m, 2H), 4.74–4.34 (m, 1H), 3.66–3.25 (m, 3H), 2.37–1.74 (m, 9H), 0.88 (ddd, *J* = 7.1, 5.0, 2.7 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 195.5, 169.5, 169.1, 142.9, 142.8, 141.0, 140.3, 135.6, 135.5, 135.4, 128.8, 128.7, 116.0, 116.0, 88.1, 87.8, 86.9, 80.3, 80.1, 78.9, 78.8, 77.1, 76.8, 73.4, 72.8, 69.9, 69.1, 68.9, 34.6, 34.5, 34.5, 33.5, 30.8, 30.3, 30.3, 29.6, 21.0, 20.8, 18.3, 18.2, 17.9, 17.5, 17.3, 17.1. HRMS (APCI+) *m*/*z*: $[M - OAc]^+$ calcd $C_{14}H_{21}O_3$ 237.1485; found 237.1492.

2-Methyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-epoxyazulen-4-one (10a)

Acetoxypyranone **9a** (19 mg, 79.6 μmol) was dissolved in CH_3CN (4 mL) to 0.02 M and transferred to a dried sealed tube and then *N*-methylpyrrolidine (NMP) (12.5 μL, 120 μmol) was added. The reaction tube was sealed, placed in an oil bath at 150 °C, and stirred for 3 h. Upon completion, the sealed tube was cooled to 23 °C, and the crude cycloadduct was filtered over a silica plug and flushed with EtOAc (3×), and then concentrated under reduced pressure to afford **10a** along with its minor diastereomer (13.5 mg, 95% yield) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.12 (ddd, *J* = 29.0, 9.7, 4.4 Hz, 1H), 5.95 (dd, *J* = 9.7, 2.5 Hz, 1H), 4.90 (ddd, *J* = 57.8, 6.6, 4.4 Hz, 1H), 2.74 (ddd, *J* = 13.6, 7.5, 1.6 Hz, 1H), 2.38–2.09 (m, 3H), 2.04–1.96 (m, 1H), 1.91 (ddd, *J* = 12.0, 6.6, 5.3 Hz, 1H), 1.27–1.15 (m, 2H), 1.06 (dd, *J* = 10.6, 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 152.4, 151.6, 126.3, 125.6, 98.7, 77.6, 75.5, 46.3, 43.8, 42.8, 39.8, 39.7, 38.5, 37.6, 37.1, 35.3, 33.0, 29.7, 19.4, 18.8. HRMS (APCI+) *m*/*z*: $[M + H]^+$ calcd $C_{11}H_{14}O_2$ 179.1067; found 179.1074.

2-Phenyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-epoxyazulen-4-one (10b)

The reaction was conducted according to the procedure described for **10a** with acetoxypyranone **9b** (24 mg, 80.0 μmol) and NMP (12.5 μL, 120 μmol) in CH_3CN (4 mL). The reaction was stirred for 4 h. Cycloadduct **10b** along with its minor diastereomer (19.2 mg, 99% yield) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.27 (m, 5H), 7.24–7.19 (m, 2H), 6.02 (d, *J* = 9.7 Hz, 1H), 5.03 (dd, *J* = 6.3, 4.5 Hz, 1H), 3.41 (tdd, *J* = 12.5, 7.8, 5.2 Hz, 1H), 3.07 (ddd, *J* = 13.7, 7.8, 1.6 Hz, 1H), 2.54–2.38 (m, 2H), 2.14–1.94 (m, 3H), 1.81–1.70 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 152.6, 142.9, 128.5, 127.0, 126.5, 125.7, 97.9, 77.8, 49.8, 46.1, 42.1, 38.1, 35.2. HRMS (APCI+) *m*/*z*: $[M + H]^+$ calcd $C_{16}H_{17}O_2$ 241.1223; found 241.1234.

2-Isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-epoxyazulen-4-one (10c)

The reaction was conducted according to the procedure described for **10a** with acetoxypyranone **9c** (21.3 mg, 80 μmol) and NMP (12.5 μL, 120 μmol) in CH_3CN (4 mL). The reaction was stirred for 7 h, and **10c** along with its minor diastereomer (16.5 mg, 99% yield) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 9.7, 4.5 Hz, 1H), 5.96 (d, *J* = 9.7 Hz, 1H), 4.94 (dd, *J* = 6.6, 4.5 Hz, 1H), 2.76 (ddd, *J* = 13.6, 7.7, 1.6 Hz, 1H), 2.30 (dtd, *J* = 11.0, 7.8, 5.0 Hz, 1H), 2.23–2.15 (m, 1H), 1.99 (dd, *J* = 12.0, 8.3 Hz, 1H), 1.89 (dddd, *J* = 24.2, 12.7, 7.2, 5.2 Hz, 2H), 1.50 (dp, *J* = 8.3, 6.6 Hz, 1H), 1.30–1.16 (m, 2H), 0.91 (dd, *J* = 11.9, 6.7 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 152.5, 125.6, 98.2, 77.4, 52.4, 45.9, 39.2, 35.4, 35.1, 33.3, 21.4, 21.4. HRMS (APCI+) *m*/*z*: $[M + H]^+$ calcd $C_{13}H_{19}O_2$ 207.1385; found 207.1390.

3-Methyl-1,3,4,8,9,9a-hexahydro-4a,8-epoxybenzo[7]annulen-5(2*H*)-one (10d)

The reaction was conducted according to the procedure described for **10a** with acetoxypyranone **9d** (20.2 mg, 0.12 mmol) and NMP (19 μL, 0.18 mmol) in CH_3CN (6 mL). The reaction was stirred for 21 h, and **10d** along with its minor diastereomer (22.6 mg, 99% yield) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.45–7.18 (m, 2H), 5.93 (dd, *J* = 39.3, 9.7 Hz, 1H), 4.77–4.69 (m, 1H), 2.11–1.93 (m, 3H), 1.92–1.78 (m, 3H), 1.77–1.51 (m, 2H), 1.33–1.17 (m, 3H), 0.98 (dd, *J* = 29.5, 6.6 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.8, 155.6, 153.0, 125.9, 125.5, 89.6, 72.6, 71.5, 40.1, 36.6, 35.5, 34.9, 34.2, 32.5, 32.3, 32.0, 28.1, 26.6, 26.1, 24.5, 23.0, 22.4. HRMS (APCI+) *m*/*z*: $[M + H]^+$ calcd $C_{12}H_{17}O_2^+$ 193.1223; found 193.1222.

3-Methyl-1,3,4,8,9,9a-hexahydro-5*H*-4a,8-epoxycyclohepta[*c*]pyran-5-one (10e)

The reaction was conducted according to the procedure described for **10a** with acetoxypyranone **9e** (15 mg, 59.4 μmol) and NMP (9 μL, 86.6 μmol) in CH_3CN (3 mL). The reaction was stirred for 8 h, and **10e** along with its minor diastereomer (10 mg, 88% yield) was isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.45–7.40 (m, 1H), 6.03 (dd, *J* = 9.7, 0.9 Hz, 1H), 4.79 (dd, *J* = 7.5, 4.8 Hz, 1H), 4.09 (dd, *J* = 11.6, 7.0 Hz, 1H), 3.55 (dtdd, *J* = 9.6, 6.0, 4.4, 2.7 Hz, 1H), 2.40 (dd, *J* = 15.1, 12.0 Hz, 1H), 2.11–2.03 (m, 1H), 1.93 (ddt, *J* = 12.6, 8.1, 1.1 Hz, 1H), 1.78–1.68 (m, 2H), 1.25–1.23 (m, 3H). ^{13}C NMR (12 MHz, $CDCl_3$) δ 196.5, 155.1, 126.2, 87.2, 72.0, 70.4, 69.0, 34.9, 33.8, 32.1, 21.6. HRMS (ESI+) *m*/*z*: $[M + H]^+$ calcd $C_{11}H_{15}O_3$ 195.1021; found 195.1015.

3-Phenyl-1,3,4,8,9,9a-hexahydro-5*H*-4a,8-epoxycyclohepta[*c*]pyran-5-one (10f)

The reaction was conducted according to the procedure described for **10a** with acetoxypyranone **9f** (15.8 mg, 50 μmol) and NMP (8 μL, 76.8 μmol) in CH_3CN (2.5 mL). The reaction was stirred for 3 h, and **10f** along with its minor diastereomer (9.6 mg, 75% yield) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 9.7, 4.8 Hz, 1H), 7.43–7.22 (m, 5H), 6.05 (d, J = 9.7 Hz, 1H), 5.04–4.79 (m, 1H), 4.50 (dd, J = 12.3, 2.9 Hz, 1H), 4.27 (dd, J = 11.7, 7.1 Hz, 1H), 3.42 (dd, J = 11.8, 10.5 Hz, 1H), 2.75 (dd, J = 15.2, 12.4 Hz, 1H), 2.21 (dtd, J = 10.4, 7.5, 2.9 Hz, 1H), 2.04–1.95 (m, 2H), 1.80 (ddd, J = 12.5, 7.5, 2.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 154.9, 141.9, 128.4, 127.6, 126.1, 125.8, 87.2, 74.9, 72.0, 70.7, 34.9, 33.8, 32.2. HRMS (ESI+) *m*/*z*: [M + H]$^+$ calcd $C_{16}H_{17}O_3$ 257.1172; found 257.1174.

3-Isopropyl-1,3,4,8,9,9a-hexahydro-5*H*-4a,8-epoxycyclohepta[*c*]pyran-5-one (10g)

The reaction was conducted according to the procedure described for **10a** with acetoxypyranone **9g** (13.5 mg, 48.0 μmol) and NMP (7.5 μL, 72.1 μmol) in CH_3CN (2.4 mL). The reaction was stirred for 5 h, and **10g** along with its minor diastereomer (10.2 mg, 96% yield) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (ddd, J = 9.7, 4.8, 0.7 Hz, 1H), 7.27 (dd, J = 9.7, 4.4 Hz, 0H), 6.10–6.06 (m, 1H), 4.85 (dd, J = 7.5, 4.8 Hz, 1H), 4.16 (dd, J = 11.6, 6.9 Hz, 1H), 3.25 (dd, J = 11.7, 10.3 Hz, 1H), 3.18 (ddd, J = 12.2, 6.7, 2.8 Hz, 1H), 2.47 (dd, J = 15.0, 12.3 Hz, 1H), 2.20–2.08 (m, 1H), 1.98 (dd, J = 12.4, 8.1 Hz, 1H), 1.85–1.74 (m, 3H), 0.99 (dd, J = 26.6, 6.8 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 154.9, 126.2, 87.3, 77.8, 72.0, 70.4, 34.9, 34.2, 33.1, 27.4, 18.6, 18.2. HRMS (ESI+) *m*/*z*: [M + H]$^+$ calcd $C_{13}H_{19}O_3$ 223.1334; found 223.1332.

3-(*tert*-Butyl)-1,3,4,8,9,9a-hexahydro-5*H*-4a,8-epoxycyclohepta[*c*]pyran-5-one (10h)

The reaction was conducted according to the procedure described for **10a** with acetoxypyranone **9h** (12.4 mg, 41.8 μmol) and NMP (6.5 μL, 62.5 μmol) in CH_3CN (2.1 mL). The reaction was stirred for 6 h, and **10h** along with its minor diastereomer (9.3 mg, 94% yield) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (ddd, J = 9.7, 4.8, 0.7 Hz, 1H), 6.08 (dd, J = 9.7, 0.7 Hz, 1H), 4.85 (dd, J = 7.5, 4.8 Hz, 1H), 4.18 (dd, J = 11.6, 7.0 Hz, 1H), 3.27 (dd, J = 11.6, 10.1 Hz, 1H), 3.15 (ddd, J = 12.5, 2.7, 0.7 Hz, 1H), 2.57–2.47 (m, 1H), 2.10 (ddd, J = 10.3, 7.5, 3.0 Hz, 1H), 1.98 (ddt, J = 12.4, 8.1, 1.0 Hz, 1H), 1.84–1.74 (m, 2H), 0.98 (d, J = 0.7 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 154.9, 126.2, 87.6, 80.3, 72.1, 70.7, 34.8, 34.1, 25.8, 25.5, 24.8. HRMS (APCI+) *m*/*z*: [M + H]$^+$ calcd $C_{14}H_{21}O_3$ 237.1491; found 237.1492.

3-Benzyl-1,3,4,8,9,9a-hexahydro-5*H*-4a,8-epoxycyclohepta[*c*]pyran-5-one (10i)

The reaction was conducted according to the procedure described for **10a** with acetoxypyranone **9i** (5.6 mg, 17.0 μmol) and NMP (2.7 μL, 26.0 μmol) in CH_3CN (0.85 mL). The reaction was stirred for 4 h, and **10i** along with its minor diastereomer (2.7 mg, 59% yield) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (dd, J = 9.7, 4.8 Hz, 1H), 7.29–7.17 (m, 5H), 6.01 (d, J = 9.7 Hz, 1H), 4.80–4.74 (m, 1H), 4.09 (dd, J = 11.7, 7.0 Hz, 1H), 3.73–3.64 (m, 1H), 3.19 (dd, J = 11.7, 10.4 Hz, 1H), 2.95 (dd, J = 13.8, 7.2 Hz, 1H), 2.73 (dd, J = 13.8, 6.1 Hz, 1H), 2.46 (dd, J = 15.1, 12.0 Hz, 1H), 2.14–2.06 (m, 1H), 1.92 (ddd, J = 12.5, 8.1, 1.2 Hz, 1H), 1.78–1.69 (m, 2H), 1.52–1.41 (m, 2H), 1.26 (s, 10H), 0.90–0.86 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.4, 154.9, 138.1, 129.6, 129.4, 128.3, 126.3, 126.1, 87.1, 73.8, 72.0, 70.3, 54.5, 42.5, 34.8, 34.1, 31.9, 30.1, 29.7, 29.4, 22.7, 18.7, 17.4, 14.1. HRMS (APCI+) *m*/*z*: [M + H]$^+$ calcd $C_{17}H_{19}O_3$ 271.1329; found 271.1328.

4-Methyl-1,4,5,9,10,10a-hexahydro-5a,9-epoxycyclohepta[*d*]oxepin-6(2*H*)-one (10j)

Acetoxypyranone **9j** (6.7 mg, 25.0 μmol) was dissolved in CH_3CN (2.5 mL) to 0.01 M and transferred to a dried sealed tube and then 2,2,6,6-tetramethylpiperidine (TMP) (17 μL, 101 μmol) was added. The reaction tube was sealed, placed in an oil bath at 150 °C, and stirred for 18 h. Upon completion of the reaction, the sealed tube was cooled to 23 °C, and the crude cycloadduct was filtered over a silica plug and flushed with EtOAc (3×), and then concentrated *in vacuo* to give **10j** and its diastereomer (3.5 mg, 67% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (dt, J = 9.6, 4.7 Hz, 1H), 5.92 (dd, J = 9.7, 8.6 Hz, 1H), 4.80 (ddd, J = 37.6, 6.9, 4.4 Hz, 1H), 4.09–3.96 (m, 1H), 3.92–3.81 (m, 1H), 3.62 (dd, J = 13.0, 10.2 Hz, 0H), 3.42 (ddd, J = 12.7, 11.0, 0.9 Hz, 1H), 2.48–2.37 (m, 1H), 2.32 (dd, J = 15.8, 9.8 Hz, 0H), 2.27–2.14 (m, 2H), 2.10–1.95 (m, 2H), 1.91–1.75 (m, 2H), 1.31–1.20 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.8, 198.4, 152.6, 152.2, 125.3, 125.2, 88.6, 88.6, 74.0, 73.8, 72.5, 70.9, 70.7, 65.2, 42.2, 39.2, 38.4, 38.3, 35.7, 35.1, 33.5, 29.7, 29.3, 23.6, 23.2. HRMS (ESI+) *m*/*z*: [M + H]$^+$ calcd $C_{17}H_{19}O_3$ 209.1178; found 209.1168.

4-Phenyl-1,4,5,9,10,10a-hexahydro-5a,9-epoxycyclohepta[*d*]oxepin-6(2*H*)-one (10k)

The reaction was conducted according to the procedure described for **10j** with acetoxypyranone **9k** (10 mg, 32.9 μmol) and TMP (2.5 μL, 148 μmol) in CH_3CN (3.3 mL). The reaction was stirred for 80 h, and **10k** and its diastereomer (3.1 mg, 33% yield) were isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54–7.50 (m, 1H), 7.38–7.29 (m, 4H), 7.23 (ddd, J = 9.6, 7.0, 4.4 Hz, 1H), 5.95 (dd, J = 9.7, 8.1 Hz, 1H), 5.06–4.74 (m, 2H), 4.20–3.97 (m, 1H), 3.68 (ddd, J = 109.3, 12.8, 10.6 Hz, 1H), 2.74–2.48 (m, 2H), 2.39–2.02 (m, 4H), 1.95–1.84 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.8, 198.1, 152.7, 152.2, 144.2, 143.6, 128.4, 128.3, 127.3, 127.1, 126.0, 125.5, 125.3, 125.3, 88.6, 79.3, 73.9, 72.6, 71.1, 65.6, 43.6, 42.3, 40.2, 38.5, 38.4, 35.7, 35.3, 33.8, 29.7. HRMS (APCI+) *m*/*z*: [M + H]$^+$ calcd $C_{17}H_{19}O_3$ 271.1329; found 271.1329.

4-Isopropyl-1,4,5,9,10,10a-hexahydro-5a,9-epoxycyclohepta[*d*]oxepin-6(2*H*)-one (10l)

The reaction was conducted according to the procedure described for **10j** with acetoxypyranone **9l** (10 mg, 32.9 μmol) and TMP (2.5 μL, 2.5 μmol) in CH_3CN (3.3 mL). The reaction was stirred for 80 h, and **10l** and its diastereomer (3 mg, 40% yield) were isolated as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.19 (dd, J = 9.7, 4.5 Hz, 1H), 5.92 (dd, J = 19.0, 9.7 Hz, 1H), 4.81 (ddd, J = 37.7, 6.8, 4.5 Hz, 1H), 4.09–3.85 (m, 1H), 3.70–3.33 (m, 2H), 2.49–2.35 (m, 1H), 2.33–2.12 (m, 3H), 2.08–1.94 (m, 2H), 1.90–1.68 (m, 4H), 0.99–0.89 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.7, 198.7, 152.5, 152.0, 125.4, 89.0, 88.6, 81.6, 79.1, 73.8, 72.6, 71.0, 65.5, 42.1, 38.5, 38.2, 35.9, 34.9, 34.4, 34.1, 33.8, 33.5, 29.7, 18.8, 18.6, 17.8, 17.3. HRMS (ESI+) m/z: $[M + H]^+$ calcd $C_{14}H_{21}O_3$ 237.1491; found 237.1479.

Conflicts of interest

There is no conflict of interest.

Data availability

The authors confirm that the data supporting these studies are available within the article and its supplementary information (SI). Supplementary information: crystallographic data collection and refinement statistics. See DOI: https://doi.org/10.1039/d5ob01429h.

CCDC 2411050 (**10b**), 2470759 (**10e**) and 2408404 (**10f**) contain the supplementary crystallographic data for this paper.[42,43a,b]

Acknowledgements

Financial support for this work was provided by the National Institutes of Health (Grant AI150466). NMR and mass spectrometry were all performed using shared resources which are partially supported by the Purdue Center for Cancer Research through NIH grant (P30CA023168).

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