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A Dihydroxylation Based Approach for the Asymmetric Syntheses of Hydroxy-γ-butyrolactones
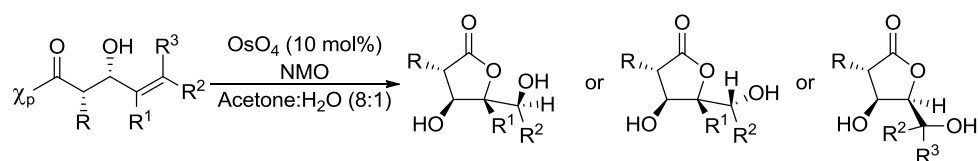
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Abstract

A method of preparing enantiopure hydroxy-γ-butyrolactones containing multiple contiguous stereocentres in high yield with good diastereoselectivity has been developed. Osmium tetroxide mediated dihydroxylation of a range of β-alkenyl-β-hydroxy-*N*-acyloxazolidin-2-ones results in formation of triols that undergo spontaneous intramolecular 5-*exo*-trig cyclisation reactions to provide hydroxy-γ-butyrolactones. The stereochemistry of these hydroxy-γ-butyrolactones has been established using NOE spectroscopy, which revealed that 1-substituted, 1,1-disubstituted, (*E*)-1,2-disubstituted, (*Z*)-1,2-disubstituted, and 1,1,2-trisubstituted alkenes undergo dihydroxylation with *anti*-diastereoselectivity, whilst 1,2,2-trisubstituted systems afford *syn*-diastereoisomers. The synthetic utility of this methodology has been demonstrated for the asymmetric synthesis of the natural product 2-deoxy-D-ribonolactone.

Introduction

Enantiomerically pure trisubstituted γ-butyrolactones are found as fragments in a large number of natural products that display a broad range of biological activities[1] and a wide range of methodology has been developed for their asymmetric synthesis.[2] Hydroxy-γ-butyrolactones represent an important subset of this type of natural product[3] and they have also been shown to be important chiral building blocks for natural product synthesis.[4] For example, Nicolaou *et al.* have employed a substituted 5-hydroxy-γ-butyrolactone as an intermediate for the synthesis of the antibiotic abyssomicin C.[4c] Shioiri *et al.* also employed a trisubstituted γ-butyrolactone as a key intermediate for the stereoselective synthesis of the C_{20}-C_{25} subunit of calyculin A.[4f] Chamberlin *et al.* used functionalised hydroxy-γ-butyrolactones as key chiral building blocks for the enantioselective synthesis of the polyketide 9*S*-dihydroerythronolide A seco acid.[4g]

A number of asymmetric methods exist for the synthesis of highly substituted hydroxy-γ-butyrolactones,[5] with a number of these approaches based upon the diastereoselective reaction of substituted enolates with appropriately substituted electrophiles. For example, Johnson *et al.* prepared substituted silyl-protected 3-hydroxy-γ-butyrolactones *via* double Reformatsky reactions, which involved reaction of a zinc propionate enolate with silyl glyoxylates to afford a new zinc enolate intermediate that then reacts further with an aryl ketone electrophile.[5d] Baba *et al.* have shown that indium enolates of α-substituted-α-bromo esters undergo diastereoselective Reformatsky reactions with α-hydroxy ketones to form 3-hydroxy-γ-butyrolactones that contain three contiguous stereocentres in good yield and with high diastereoselectivity.[5i] Luo and Gong *et al.* prepared trisubstituted 2-hydroxy-γ-

butyrolactones by performing enantioselective aldol reactions between ketones and α-keto acids using a proline derived organocatalyst, with subsequent diastereoselective reduction of the resulting ketone functionality to afford the desired γ-butyrolactones with high levels of diastereocontrol.[5f]

Another common method of forming highly substituted hydroxy-γ-butyrolactones is through dihydroxylation of γ,δ-unsaturated carbonyl systems, with spontaneous intramolecular ring-closure then occurring to afford a γ-butyrolactone skeleton. For example, Woerpel *et al.* carried out osmium tetroxide (OsO$_4$) catalysed directed dihydroxylation reactions of α-hydroxy-γ,δ-unsaturated acids to afford hydroxy-γ-butyrolactones as single diastereoisomers in good yield.[5c] Brückner *et al.* have used Sharpless asymmetric dihydroxylation reactions of disubstituted[5m] and trisubstituted[5g] β,γ-unsaturated esters to prepare substituted 3-hydroxy-γ-butyrolactones in reasonable yield with low to moderate levels of enantiomeric excess (ee). Jenkinson *et al.* prepared synthetically useful and highly functionalised sugar-lactones using directed osmium dihydroxylations of chain extended ribulose and erythrose derivatives.[5b]

We have previously reported that β-alkenyl-β-hydroxy-*N*-acyloxazolidin-2-ones (**1**) undergo efficient epoxidation/lactonisation reactions with catalytic VO(acac)$_2$ and a stoichiometric equivalent of *tert*-butylhydroperoxide to afford hydroxy-γ-butyrolactones (**3**) (Scheme 1). It is proposed that an unstable epoxide (**2**) is generated with high levels of diastereocontrol, which is then ring-opened by intramolecular nucleophilic attack of the exocyclic carbonyl fragment that gives clean inversion of configuration at the C_5 position. Hydrolysis of the

resulting iminium species affords a highly functionalised hydroxy-γ-butyrolactone skeleton containing multiple contiguous stereocentres.[6]
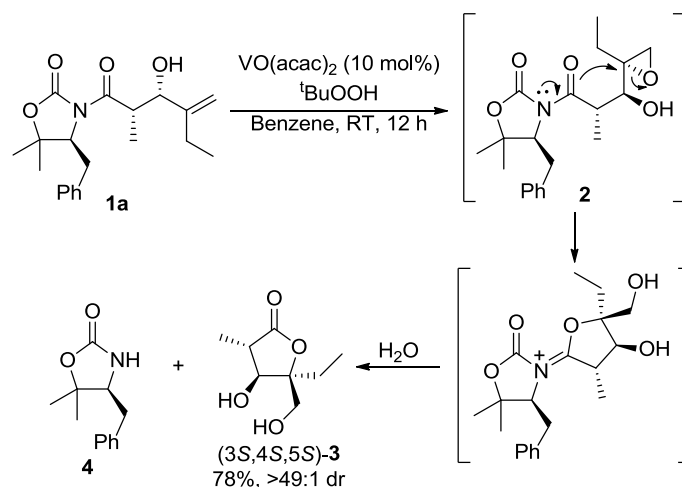
Scheme 1. Epoxidation/lactonisation sequence with inversion of configuration at C_5 to form a hydroxy-γ-butyrolactone **3** containing three contiguous stereocentres.

As this epoxidation/lactonisation sequence leads to inversion of configuration at the C_5 position, it was decided to investigate an osmium catalysed dihydroxylation/lactonisation protocol in order to access complementary diastereoisomers of this type of hydroxy-γ-butyrolactone (Scheme 2). For example, dihydroxylation of the alkene fragment of the generic aldol substrate **1** with *anti*-diastereoselectivity to its β-hydroxyl group would afford a triol (**5**), which would spontaneously lactonise to afford a diastereomeric hydroxy-γ-butyrolactone.
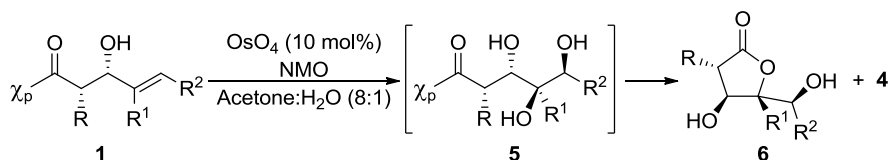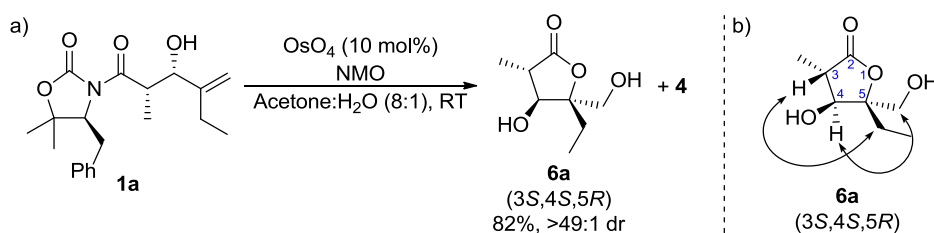
Scheme 2. Proposed dihydroxylation/lactonisation of unsaturated aldols (**1**) to produce hydroxy-γ-butyrolactones (**6**).

Therefore, we now report herein a highly diastereoselective dihydroxylation based approach for the synthesis of functionalised hydroxy-γ-butyrolactones containing multiple contiguous stereocentres, where the major diastereoisomer of the lactone produced is controlled by the alkene substitution pattern.

Results and Discussion

The configuration of hydroxy-γ-butyrolactone **3**, formed from the epoxidation/lactonisation reaction of aldol **1a** had previously been unequivocally assigned as (3*S*,4*S*,5*S*) using X-ray crystallographic analysis. Consequently, it was decided to investigate the corresponding dihydroxylation/lactonisation reaction of aldol **1a** to confirm that a different diastereoisomer of hydroxy-γ-butyrolactone would be produced. Therefore, unsaturated aldol **1a**[7] was treated under standard Upjohn conditions[8] with 10 mol% OsO$_4$ and *N*-methylmorpholine-*N*-oxide (NMO) in acetone:H$_2$O (8:1) at room temperature to produce a *new* hydroxy-γ-butyrolactone **6a** in 69% yield and in >49:1 dr (Scheme 3a). [1]H NOE spectroscopic analysis of **6a** showed a strong interaction between the C_3 proton and the methylene protons of the C_5 ethyl group, as well as a strong interaction between the C_4 proton and the C_5 CH$_2$OH methylene protons (Scheme 3b), indicating a (3*S*,4*S*,5*R*) configuration. This assignment is consistent with the

expected suprafacial dihydroxylation of unsaturated aldol **1a** with *anti*-diastereoselectivity with respect to its β-hydroxyl group. Thus, whilst our previously reported epoxidation/lactonisation sequence produces (3*S*,4*S*,5*S*)-hydroxy-γ-butyrolactone **3**, this dihydroxylation/lactonisation sequence provides its complementary C_5 diastereoisomer (**6a**) in high dr.

Scheme 3. a) Dihydroxylation/lactonisation of unsaturated aldol **1a** to form hydroxy-γ-butyrolactone **6a**. b) Strong ^{1}H NOE interactions in γ-butyrolactone **6a** confirm a (3*S*,4*S*,5*R*) configuration.

To further investigate the scope and effect of the alkene substitution pattern on the stereochemical outcome of this dihydroxylation/lactonisation protocol, a series of *syn*-aldols (**1b-j**) was prepared in good yield and high dr by reaction of the boron enolate of 5,5-dimethyl-*N*-propionyl-oxazolidin-2-one (**7a**) with the corresponding α,β-unsaturated aldehydes (Scheme 4).[7] These *syn*-aldols (**1b-j**) were then treated with 10 mol% OsO$_4$ and NMO in acetone:H$_2$O (8:1) at room temperature to afford a series of hydroxy-γ-butyrolactones (**6b-j**) in good yield and generally high diastereoselectivity (Table 1, entries 1-9).
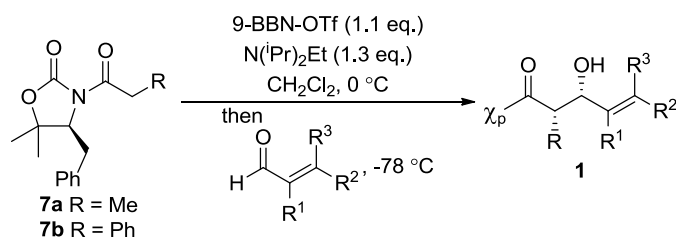
Scheme 4. SuperQuat auxiliary directed synthesis of unsaturated *syn*-aldols (**1**).

Reaction of 1,1-disubstituted aldol **1b**, which contains a terminal *O*-benzyl substituent, with 10 mol% OsO_4 and NMO proceeded with good levels of *anti*-diastereoselectivity to form hydroxy-γ-butyrolactone **6b** in high yield (Table 1, entry 1). The stereochemistry of hydroxy-γ-butyrolactone **6b** was unequivocally assigned as (3*S*,4*S*,5*R*) *via* X-ray crystallographic analysis (see supporting information). The terminal *O*-benzyl fragment of this type of lactone makes it particularly useful as a bifunctional synthetic building block for the synthesis of polyketide inspired synthetic targets.[9] The stereochemistry of the remaining lactones (**6**) was determined by ^{1}H NOE spectroscopic analysis as well as by comparison with literature precedent for each of the different substitution patterns (see below).

Table 1. Dihydroxylation of aldols **1b-k** to afford hydroxy-γ-butyrolactones **6b-k**.

| Entry	Aldol (**1b-k**)	Triol (**5b-k**) (not isolated)[a]	Lactone (**6b-k**)[a,b]	dr[c]	Yield (%)[d]
1	**1b** 78%, >95% de	**5b**	**6b**	10:1	93
2	**1c** 53%, >95% de	**5c**	**6c**	3:1	79
3	**1d** 78%, >95% de	**5d**	**6d**	9:1	81
4	**1e** 91%, >95% de	**5e**	**6e**	5:1	83
5	**1f** 89%, >95% de	**5f**	**6f**	4:1	77
6	**1g** 88%, >95% de	**5g**	**6g**	2:1	74
7	**1h** 82%, >95% de	**5h**	**6h**	>49:1	82
8	**1i** 46%, >95% de	**5i**	**6i**	>49:1	93
9	**1j** 92%, >95% de	**5j**	**6j**	5:1	41
10	**1k** 75%, >95% de	**5k**	**6k**	9:1	75

[a]Major diastereoisomer formed. [b]Configuration of hydroxyl-γ-butyrolactones confirmed by ^{1}H NOE spectroscopic analysis. [c]Determined by analysis of the crude ^{1}H NMR spectra. [d]Yields after purification by column chromatography.

The dihydroxylation/lactonisation reaction of acrolein aldol **1c** was less diastereoselective, giving a 3:1 mixture of diastereoisomers, with the major diastereoisomer (**6c**) being formed from dihydroxylation with *anti*-diastereocontrol in 79% yield (Table 1, entry 2). It was found that (*E*)-1,2-disubstituted aldols derived from cinnamaldehyde and crotonaldehyde (**1d** and **1e** respectively) underwent dihydroxylation with greater levels of *anti*-diastereoselectivity to give hydroxy-γ-butyrolactones **6d** (9:1 dr) and **6e** (5:1 dr) in good yields (Table 1, entries 3 and 4). Pleasingly, the (*E*)-1,2-disubstituted aldol **1f** containing an *O*-benzyl group also underwent dihydroxylation/lactonisation under standard Upjohn conditions to form the hydroxy-γ-butyrolactone **6f** in 77% yield with 4:1 diastereoselectivity (Table 1, entry 5). The related (*Z*)-1,2-disubstituted *O*-benzyl aldol **1g** was found to undergo dihydroxylation with poor levels of *anti*-diastereoselectivity (2:1 dr), with the corresponding hydroxy-γ-butyrolactone **6g** being formed with the opposite C_6 configuration to that observed for (*E*)-1,2-disubstituted aldol **1f** (Table 1, entry 6). Reaction of (*E*)-1,1,2-trisubstituted aldol **1h** under standard dihydroxylation/lactonisation conditions proceeded with excellent levels of *anti*-diastereoselectivity to afford hydroxy-γ-butyrolactone **6h** in 82% yield as a single diastereoisomer (Table 1, entry 7). The related *O*-benzyl (*E*)-1,1,2-trisubstituted aldol **1i** also underwent dihydroxylation/lactonisation with similar levels of high *anti*-diastereoselectivity, providing the synthetically useful *O*-benzyl-γ-butyrolactone **6i** in 93% yield as a single diastereoisomer (Table 1, entry 8). However, the reaction of 1,2,2-trisubstituted aldol **1j** derived from 3-methyl-2-butenal proceeded with reduced diastereoselectivity, with the major hydroxy-γ-butyrolactone **6j** diastereoisomer having the opposite configuration at C_5 to that observed for the previous examples. Therefore, it follows that the 1,2,2-trisubstituted aldol **1j** must preferentially undergo dihydroxylation *syn* to its β-hydroxyl group (5:1 dr) before lactonisation to afford (3*S*,4*S*,5*R*)-hydroxy-γ-butyrolactone **6j** in 41% yield (Table 1, entry 9). We then decided to investigate the effect of varying the α-substituent of the unsaturated aldol

on the dihydroxylation/lactonisation reaction. The α-phenyl 1,1-disubstituted aldol **1k** was prepared using our standard boron aldol protocol and subjected to the standard dihydroxylation/lactonisation conditions. It was found that α-phenyl aldol **1k** underwent dihydroxylation with good levels of *anti*-diastereoselectivity (9:1 dr), allowing the corresponding hydroxy-γ-butyrolactone **6k** to be isolated in 75% yield (Table 1, entry 10).

Whilst the vast majority of alkene substitution patterns gave high levels of diastereoselectivity for our dihydroxylation/lactonisation sequence, the (Z)-1,2-disubstituted aldol **1g** gave a 2:1 mixture of lactone diastereoisomers. In an attempt to improve the diastereoselectivity, (Z)-1,2-disubstituted aldol **1g** was reacted under Sharpless asymmetric dihydroxylation conditions using both AD-mix-α and AD-mix-β (Scheme 5a and b).[10] Remarkably, the 'mismatched' reaction of (Z)-1,2-disubstituted aldol **1g** with AD-mix-α resulted in dihydroxylation/lactonisation with reversal of diastereoselectivity compared with the reaction using the standard Upjohn conditions. The hydroxy-γ-butyrolactones (**6g** and **8**) were obtained in 95% yield as a 4:1 mixture of diastereoisomers, with the major lactone (**8**) being formed as the result of dihydroxylation with *syn*-diastereoselectivity with respect to the β-hydroxyl group of **1g** (Scheme 5a). This facial selectivity is consistent with that observed previously by Sharpless *et al*. for reaction of a simplified (Z)-*O*-benzyl allylic alcohol with AD-mix-α.[11] Pleasingly, the use of AD-mix-β resulted in 'matched' enhancement of the diastereoselectivity observed for dihydroxylation under Upjohn conditions, affording the hydroxy-γ-butyrolactones (**6g** and **8**) in 95% yield as a 17:1 mixture of diastereoisomers (Scheme 5b). In this case the major diastereoisomer (**6g**) obtained is the result of dihydroxylation with *anti*-diastereoselectivity relative to the β-hydroxyl group of **1g**, which is

again consistent with the results obtained by Sharpless *et al*. using AD-mix-β on related substrates.
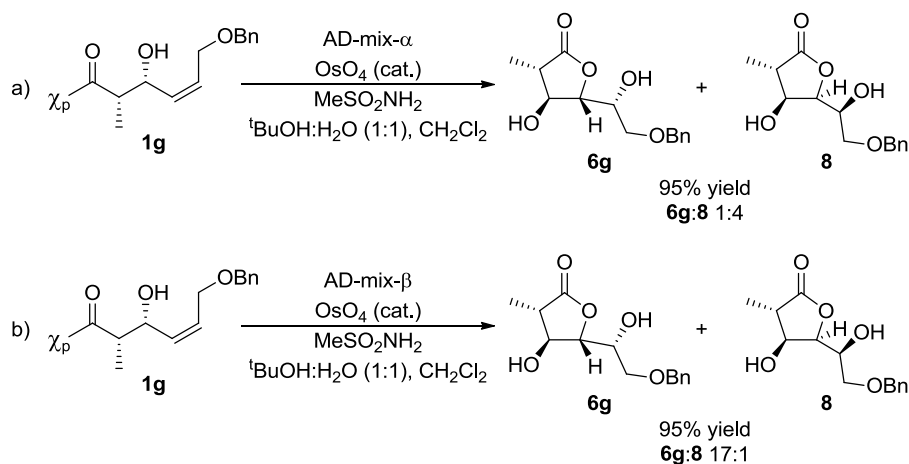
**Scheme 5**. Effect of using Sharpless asymmetric dihydroxylation conditions.

Finally, in order to demonstrate the synthetic utility of our dihydroxylation/lactonisation protocol we decided to apply it to the synthesis of 2-deoxy-D-ribonolactone (**11**),[12] which is a byproduct of oxidatively damaged DNA.[13] 2-Deoxy-D-ribonolactone (**11**) has also been shown to be a useful synthetic precursor,[14] whilst its nucleoside derivatives are of structural interest because they can potentially act as universal bases and non-hydrogen bonding isosteres of nucleobases for chemical biology applications.[15] Therefore, the boron enolate of α-chloropropionyl-*N*-acyl-oxaolidin-2-one **7c** was reacted with acrolein to afford *syn*-aldol **9** in a 45% yield and in >95% de. Treatment of the α-chloro-β-vinyl-aldol **9** with zinc dust and ammonium chloride in methanol resulted in dechlorination, providing the desired allylic alcohol **10** in 82% yield.[16] The dechlorinated alcohol **10** was then subjected to the standard Upjohn dihydroxylation/lactonisation conditions, to afford 2-deoxy-D-ribonolactone (**11**) as a 9:1 mixture of diastereoisomers in 87% yield (Scheme 6),[17] whose spectroscopic data was consistent with that reported previously.[12]
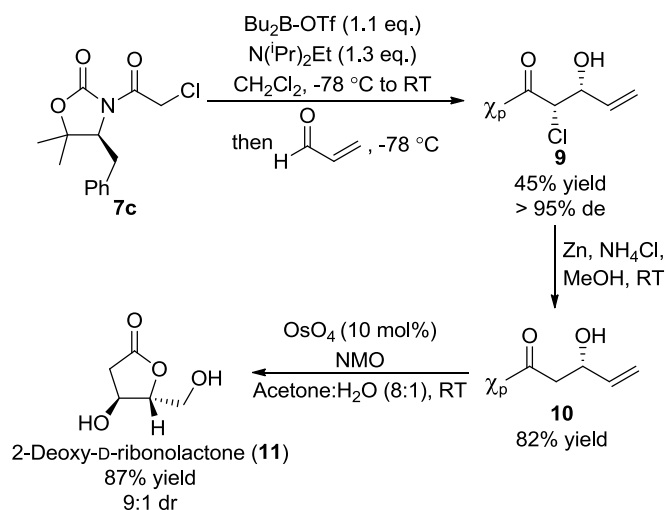
Scheme 6. Asymmetric synthesis of 2-deoxy-D-ribonolactone (**11**).

Assignment of Stereochemistry

There are many literature examples of directed dihydroxylation reactions of allylic alcohols, with selected examples of dihydroxylations of allylic alcohols with various substitution patterns shown in Scheme 7.[18] Several stereochemical models have been proposed to rationalise the observed diastereoselectivity in dihydroxylation reactions of allylic alcohols, most notably the models described by Kishi, Houk and Vedejs.[19-22]
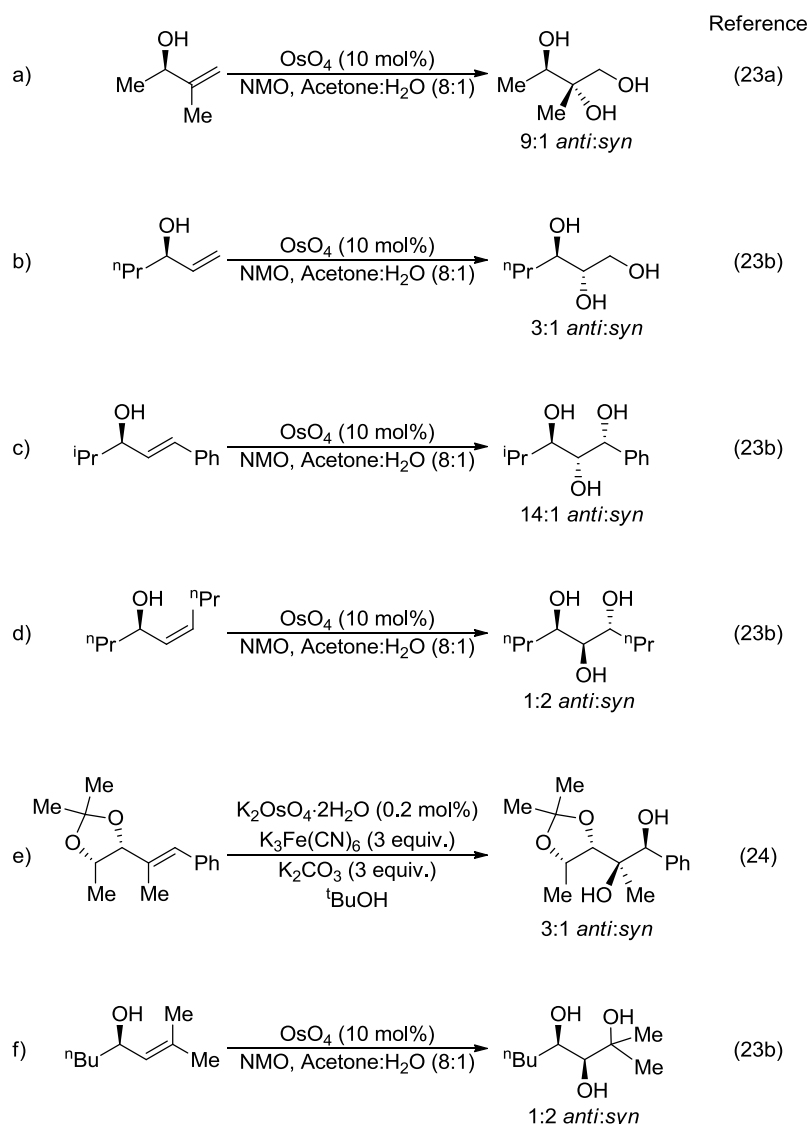
Scheme 7. Literature examples of dihydroxylation reactions of allylic alcohols with different alkene substitution patterns.

The configuration of each of the hydroxyl-γ-butyrolactone (**6a-k**) prepared in this study has been determined by ^{1}H NOE spectroscopic analysis (Figure 1) and the conclusions compared with the literature precedent for dihydroxylation of each of the alkene substitution patterns shown in Scheme 7. The results from dihydroxylation/lactonisation of 1,1-disubstituted (**1a** and **1b**), 1-substituted (**1c**), and (*E*)-1,2-disubstituted allylic alcohols (**1d-f**) are consistent with the *anti*-diastereoselectivity observed in catalytic osmylation reactions of related

substrates with the same alkene substitution patterns (Scheme 7a-c). The ^{1}H NOE spectrum of the *O*-benzyl hydroxy-γ-butyrolactone **6b**, derived from dihydroxylation/lactonisation of 1,1-disubstituted aldol **1b**, shows a strong interaction between the C_3 proton and the C_5 methylene protons of the *O*-benzyl substituent that confirms the configuration of the C_5 stereocentre (Figure 1b). The ^{1}H NOE spectra of the hydroxy-γ-butyrolactones **6c**-**f** also show strong interaction between the C_3 proton and the C_5 proton, confirming that these protons lie on the same face of the lactone ring (Figure 1c-f).

The modest levels of *anti*-diastereoselectivity (2:1) observed for the reaction of (*Z*)-1,2-disubstituted aldol **1g** are in contrast with the observations of Donohoe *et al*., who found that simple (*Z*)-1,2-disubstituted allylic alcohols gave low levels (2:1) of *syn*-diastereoselectivity when dihydroxylation was carried out under Upjohn conditions (Scheme 7d).[23b] In our case, the configuration of the C_5 stereocentre of the major diasteroisomer of hydroxy-γ-butyrolactone **6g** was confirmed by analysis of the ^{1}H NOE spectrum, which showed a strong interaction between the C_3 proton and the C_5 proton (Figure 1g). However, the low levels of diastereoselectivity observed in both cases suggest that the directing effect of the allylic alcohol in (*Z*)-1,2-disubstituted systems is limited, therefore it is unsurprising that different substrates result in different diastereoisomers being formed with poor dr.

The high levels of *anti*-diastereoselectivity observed for the (*E*)-1,1,2-trisbstututed aldols (**1h** and **1i**) were consistent with the results of Fronza *et al*. who found that an acetonide protected allylic alcohol gave dihydroxylation with *anti*-diastereoselectivity when reacted under Sharpless conditions in the absence of a chiral ligand (Scheme 7e).[24] The configuration of the hydroxy-γ-butyrolactones (**6h** and **6i**) was confirmed by analysis of the ^{1}H NOE

spectra, which showed strong interactions between the proton on C_3 and the C_5 methyl protons as well as strong interactions between the C_3 methyl group and the C_5 CHOH proton in both cases (Figure 1h and 2i).

The dihydroxylation/lactonisation of 1,2,2-trisubstituted aldol **1j** proceeded with *syn*-diastereoselectivity, which is consistent with the *syn*-diastereoselectivity previously observed by Donohoe *et. al*. for dihydroxylation of 1,2,2-trisubstituted allylic alcohols (Scheme 7f).[23b] The 5*R* stereochemistry of the major diastereoisomer of hydroxy-γ-butyrolactone **6j** was confirmed by a strong interaction in the ^{1}H NOE spectra between the methyl protons on C_3 and the C_5 proton (Figure 1j), whilst a vicinal coupling constant between the protons on C_4 and C_5 of $^3J = 7.4$ Hz is indicative of a *syn*-relationship between these protons.[25]

The α-substituent of the aldol product was shown not to affect the stereochemical outcome of the dihydroxylation reaction unduly, with α-phenyl 1,1-disubstituted aldol **1k** undergoing dihydroxylation with the expected *anti*-diastereoselectivity (Scheme 7a) to afford hydroxy-γ-butyrolactone **6k**, which exhibited the same characteristic interactions in its ^{1}H NOE spectrum as the previous examples (Figure 1k).
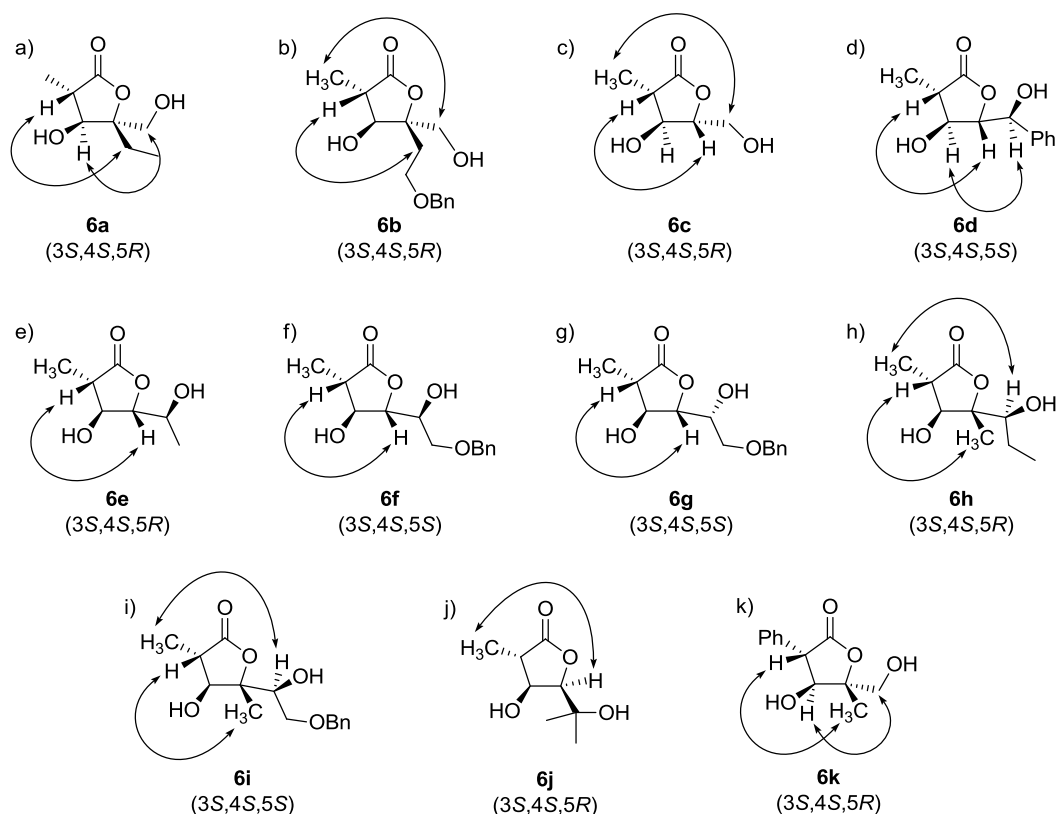
**Figure 1**. Strong interactions in the ^{1}H NOE spectra of the hydroxyl-γ-butyrolactones (**6a-k**).

Of particular relevance to the results described is the previous report of Dias *et al.*, who reported the dihydroxylation/lactonisation of a small series of closely related Evans derived β-alkenyl-*O*-silyl aldol products (**14a-d**). Surprisingly, the configuration of the resulting *O*-silyl-γ-butyrolactones (**16a-d**) was reported as (3*S*,4*S*,5*S*), which was different to the results we had obtained, with lactones **16b** and **16d** reported to have arisen from an unprecedented antarafacial dihydroxylation reaction occurring with *syn*-diastereoselectivity to the β-*O*-silyl hydroxyl group (Scheme 9).[5h,26] Therefore, in order to investigate the effect of the *O*-silyl group on these dihydroxylation/lactonisation reactions, unsaturated aldol **1a** was *O*-TBS protected using TBS-OTf and 2,6-lutidine and subjected to the standard Upjohn dihydroxylation/lactonisation conditions, which gave *O*-TBS γ-butyrolactone **13** in a 3:1 dr.

This mixture was then deprotected using TBAF to give hydroxy-γ-butyrolactone **6a** in 65% yield and 3:1 dr (Scheme 8), whose ^{1}H, ^{13}C{^{1}H}, and NOE spectra were identical to those of the lactone we had previously formed from dihydroxylation/lactonisation of the unprotected aldol **1a**.
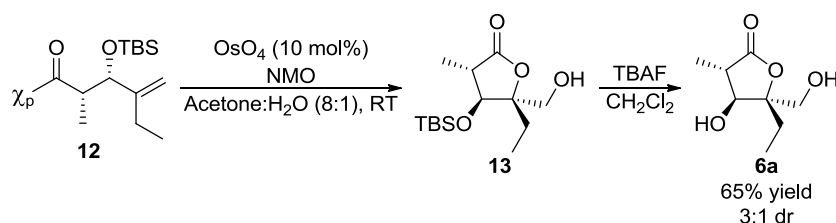
Scheme 8. Dihydroxylation/lactonisation of unprotected aldol **1a** and *O*-TBS aldol **12** afford the same major diastereoisomer of hydroxy-γ-butyrolactone (**6a**).

In light of this result, we propose that both the free hydroxyl and *O*-silyl protected unsaturated aldol derivatives of **1a** undergo dihydroxylation with *anti*-diastereoselectivity to the stereodirecting group. We therefore suggest that the stereochemical assignments of the *O*-silyl-γ-butyrolactones (**16a-d**) previously reported by Dias *et al.*[5h] are incorrect and propose that the configuration of these lactones be reassigned as shown in Scheme 9.
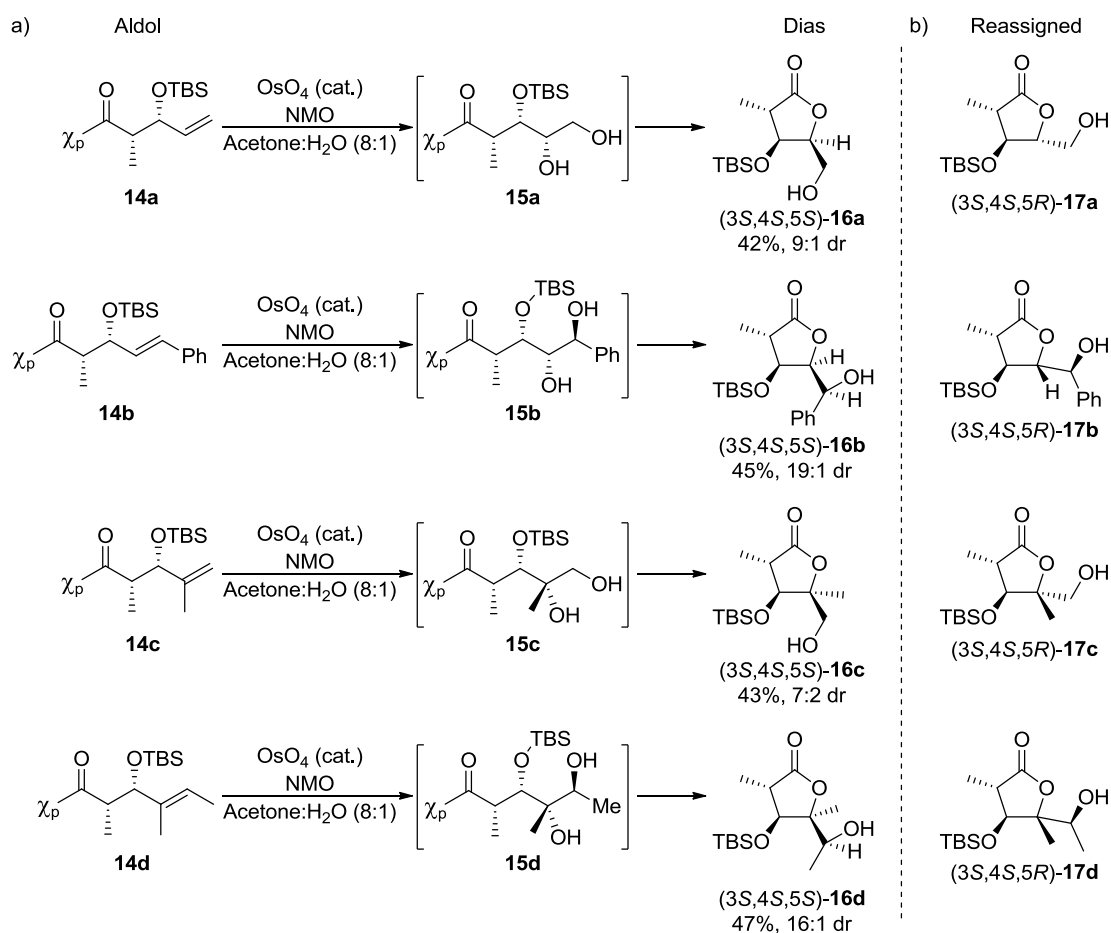
Scheme 9. a) Dias *et al.*'s dihydroxylation/lactonisation of *O*-TBS protected unsaturated aldols (**14a-d**). b) Proposed reassignment of configuration of the reported *O*-silyl-γ-butyrolactones (**17a-d**).

Conclusions

We have developed a method of preparing enantiomerically pure hydroxy-γ-butyrolactones (**6a-k**) containing multiple contiguous stereocentres through directed dihydroxylation/lactonisation reactions of β-alkenyl-β-hydroxy-*N*-acyloxazolidin-2-ones (**1a-k**). The configurations of the resulting hydroxy-γ-butyrolactones (**6a-k**) have been confirmed by ^{1}H NOE spectroscopic analysis, which revealed that the diastereoselectivity of these directed dihydroxylation reactions is dependent on the alkene substitution pattern. It was found that 1-substituted, 1,1-disubstituted, (*E*)-1,2-disubstituted, (*Z*)-1,2-disubstituted, and

1,1,2-trisubstituted alkenes undergo dihydroxylation with *anti*-diastereoselectivity to their β-hydroxyl groups, whereas a 1,2,2-trisubstituted alkene gave the *syn*-diastereoisomer. The poor levels of diastereoselectivity observed for the dihydroxylation/lactonisation of the (*Z*)-1,2-disubstituted aldol (**1g**) could be improved using Sharpless' asymmetric dihydroxylation conditions, with the 'matched' and 'mismatched' diastereoisomers being formed dependent on the enantiomer of ligand used. The synthetic utility of this directed dihydroxylation/lactonisation methodology has been demonstrated with a short synthesis of 2-deoxy-D-ribonolactone (**11**).

Experimental

General: All reactions were performed using starting materials and solvents obtained from commercial sources without further purification using dry solvents under an atmosphere of nitrogen. ^{1}H NMR spectra were recorded at 250, 300, 400 and 500 MHz and ^{13}C{^{1}H} NMR spectra were recorded at 75 MHz. Chemical shifts δ are quoted in parts per million and are referenced to the residual solvent peak. NMR peak assignments were confirmed using 2D ^{1}H COSY where necessary. Chemical shift is reported in parts per million (ppm) and all coupling constants, *J*, are reported in Hertz (Hz). Infra-red spectra were recorded as thin films or were recorded with internal background calibration in the range 600-4000 cm^{-1}, using thin films on NaCl plates (film), or KBr discs (KBr) as stated. High resolution mass spectra were recorded in either positive or negative mode using electrospray (ES) ionisation. Optical rotations were recorded with a path length of 1 dm; concentrations (*c*) are quoted in g/100 mL.

General Procedure for the Acylation of (*S*)-4-Benzyl-5,5-dimethyloxazolidin-2-one: *n*-BuLi (1.1 equiv., 2.5 M solution in hexane) was added to a solution of (*S*)-4-benzyl-5,5-

dimethyloxazolidin-2-one (1 equiv.) in dry THF at -78°C under nitrogen and was stirred for 30 minutes. The appropriate acid chloride (1.1 equiv.) was added in one portion and the resulting solution was stirred for a further two hours. The reaction was quenched with saturated ammonium chloride and allowed to warm to ambient temperature. The THF was evaporated under reduced pressure, the resulting oil was redissolved in dichloromethane and extracted with brine. The combined organic extracts were dried over $MgSO_4$ and concentrated to afford the crude product.

(S)-4-Benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one, 7a: The title compound was prepared according to the general procedure from n-BuLi (6.43 mL, 16.1 mmol, 2.5 M solution in hexane), (S)-4-benzyl-5,5-dimethyloxazolidin-2-one (3.00 g, 14.6 mmol) and propionyl chloride (1.40 mL, 16.1 mmol) in THF (90 mL). The crude product was purified by recrystallisation from diethyl ether and hexane to afford (S)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a** (3.52 g, 13.4 mmol, 92%) as a white solid. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.31-7.17 (5H, m, Ph), 4.48 (1H, dd, J = 9.6, 3.9 Hz, CHN), 3.12 (1H, dd, J = 14.3, 3.9 Hz, CH$H_A$$H_B$Ph), 2.94-2.81 (3H, m, CH$_A$$H_BPh, COCH_2$), 1.34 (3H, s, C(C$H_3$)(CH$_3$)), 1.33 (3H, s, C(CH$_3$)(C$H_3$)), 1.12 (3H, t, J = 7.33 Hz, CH$_2$CH_3); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 174.4, 152.8, 137.1, 129.2, 128.8, 126.9, 82.3, 63.6, 35.5, 29.5, 28.7, 22.4, 8.5; IR cm^{-1} ν = 1766 (C=O$_{ox}$), 1703 (C=O); HRMS: m/z (ES) 262.1446, $C_{15}H_{20}NO_3$ [M+H]$^+$ requires 262.1443; $[\alpha]_D^{21}$ = -42.0 (c = 0.50 g/100 mL in CHCl$_3$).

(S)-4-Benzyl-5,5-dimethyl-3-(2-phenylacetyl)oxazolidin-2-one, 7b: The title compound was prepared according to the general procedure from n-BuLi (1.71 mL, 4.3 mmol, 2.5 M solution in hexane), (S)-4-benzyl-5,5-dimethyloxazolidin-2-one (0.80 g, 3.9 mmol) and phenylacetyl chloride (0.56 mL, 4.3 mmol) in THF (30 mL). The crude product was purified using flash silica chromatography [CH$_2$Cl$_2$, R$_f$ 0.61] to afford (S)-4-benzyl-5,5-dimethyl-3-(2-

phenylacetyl)oxazolidin-2-one **7b** (0.96 g, 3.0 mmol, 76%) as a colourless oil, which solidified on standing. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.33-7.15 (10H, m, Ph$_{ox}$, Ph), 4.46 (1H, dd, J = 9.6, 3.8 Hz, C*H*N), 4.25 (2H, s, COC*H*$_2$Ph), 3.11 (1H, dd, J = 14.4, 3.8 Hz, C*H*$_A$H$_B$Ph), 2.82 (1H, dd, J = 14.4, 9.6 Hz, CH$_A$*H*$_B$Ph), 1.34 (3H, s, C(C*H*$_3$)(CH$_3$)), 1.29 (3H, s, C(CH$_3$)(C*H*$_3$)); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 171.6, 152.7, 137.0, 133.8, 129.8, 129.2, 128.8, 128.7, 127.3, 126.9, 82.5, 63.9, 41.9, 35.3, 28.7, 22.4; IR cm^{-1} ν = 1765 (C=O$_{ox}$), 1712 (C=O); HRMS: *m/z* (ES) 324.1605, C$_{20}$H$_{22}$NO$_3$ [M+H]$^+$ requires 324.1599; $[\alpha]_D^{21}$ = -36.0 (*c* = 0.50 g/100 mL in CHCl$_3$).

Non-Commercially Available Aldehydes

(*E*)-4-(Benzyloxy)but-2-enal: Based on a literature procedure,[27] oxalyl chloride (0.26 mL, 3.1 mmol) was dissolved in dry dichloromethane (10 mL) at -55 ˚C under nitrogen. Dimethylsulphoxide (0.39 mL, 5.6 mmol) was added and the resulting solution was stirred for two minutes. (*Z*)-4-(Benzyloxy)but-2-en-1-ol (0.50 g, 2.8 mmol) in dichloromethane (1 mL) was added dropwise to the solution to form a light yellow cloudy mixture, which was stirred for 15 minutes at -55 ˚C. Triethylamine (1.96 mL, 14.0 mmol) was then added and the resulting solution was stirred for a further 15 minutes at -55 ˚C. The thick white slurry was warmed to room temperature and was quenched with the addition of water (10 mL). The layers were separated and the aqueous layer was extracted three times with dichloromethane (20 mL). The combined organic layers were washed with 1 M HCl (10 mL) and saturated NaHCO$_3$ before being dried over MgSO$_4$ and concentrated. The crude product was purified using flash silica chromatography [1:8 EtOAc:Petroleum ether, R$_f$ 0.25] to predominantly afford the *cis* alkene (0.42 g, 2.4 mmol, 84%) as a colourless liquid. The pure material was dissolved in dichloromethane (1 mL) with a catalytic amount of *p*-TSA and left at room temperature overnight to isomerise to the *trans* isomer (*E*)-4-(benzyloxy)but-2-enal in a 99:1

ratio. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 9.58 (1H, d, J = 7.9 Hz, C*H*O), 7.39-7.28 (5H, m, Ph), 6.85 (1H, dt, J = 15.8, 4.1 Hz, C*H*=CHCHO), 6.41 (1H, ddt, J = 15.8, 7.9, 1.9 Hz, C*H*CHO), 4.60 (2H, s, OC*H*$_2$Ph), 4.29 (2H, dd, J = 4.1, 1.9 Hz, C*H*$_2$OBn); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 193.4, 153.2, 137.5, 131.9, 128.6, 128.1, 127.8, 73.1, 68.7; IR cm^{-1} ν = 1682 (C=O); HRMS: m/z (ES) 199.0737, C$_{11}$H$_{12}$NaO$_2$ [M+Na]$^+$ requires 199.0734.

4-(Benzyloxy)butanal: Oxalyl chloride (1.03 mL, 12.2 mmol) was dissolved in dry dichloromethane (50 mL) at -55 ˚C under nitrogen. Dimethylsulphoxide (1.58 mL, 22.2 mmol) was added and the resulting solution was stirred for 2 minutes. 4-(Benzyloxy)butan-1-ol (2.00 g, 11.1 mmol) in dichloromethane (5 mL) was added dropwise to the solution to form a light yellow cloudy mixture, which was stirred for 15 minutes at -55 ˚C. Triethylamine (7.73 mL, 55.5 mmol) was then added and the resulting solution was stirred for a further 15 minutes at -55 ˚C. The thick white slurry was warmed to room temperature and was quenched with the addition of water (50 mL). The layers were separated and the aqueous layer was extracted three times with dichloromethane (50 mL). The combined organic layers were washed with 1 M HCl (10 mL) and saturated NaHCO$_3$ before being dried over MgSO$_4$ and concentrated. The crude product was purified using flash silica chromatography [1:9 EtOAc:Petroleum ether, R$_f$ 0.63] to afford 4-(benzyloxy)butanal (1.48 g, 8.3 mmol, 75%) as a colourless liquid. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 9.68 (1H, s, C*H*O), 7.30-7.18 (5H, m, Ph), 4.41 (2H, s, OC*H*$_2$Ph), 3.43 (2H, t, J = 6.1 Hz, C*H*$_2$OBn), 2.45 (2H, t, J = 7.1 Hz, CHOC*H*$_2$), 1.87 (2H, app. quintet, J = 6.6 Hz, CH$_2$C*H*$_2$CH$_2$OBn); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 202.1, 138.3, 128.3, 127.5, 72.8, 69.0, 40.8, 22.5; IR cm^{-1} ν = 1721 (C=O); HRMS: m/z (ES) 201.0894, C$_{11}$H$_{14}$NaO$_2$, [M+Na]$^+$ requires 201.0891.

4-(Benzyloxy)-2-methylenebutanal: 4-(Benzyloxy)butanal (0.50 g, 2.8 mmol) was dissolved in 37% aqueous formaldehyde solution (0.27 mL, 3.7 mmol). Dimethylamine hydrochloride (0.30 g, 3.7 mmol) was added and the mixture was heated at 70 ˚C for 24

hours. The reaction was cooled to room temperature, quenched with saturated $NaHCO_3$, extracted into hexane and the combined organic fractions were washed with water, dried over $MgSO_4$ and concentrated. The crude product was purified using flash silica chromatography [1:9 EtOAc:Petroleum ether, R_f 0.31] to afford 4-(benzyloxy)-2-methylenebutanal (0.41 g, 2.2 mmol, 78%) as a colourless liquid. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 9.46 (1H, s, CHO), 7.30-7.19 (5H, m, Ph), 6.31 (1H, s, C=CH$_A$H$_B$), 6.00 (1H, s, C=CH$_A$H$_B$), 4.43 (2H, s, OCH_2Ph), 3.53 (2H, t, J = 6.4 Hz, CH_2OBn), 2.51 (2H, t, J = 6.4 Hz, CH$_2$=CCH_2); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 194.4, 146.9, 138.2, 135.7, 128.4, 127.6, 127.5, 72.8, 67.9, 28.2; IR cm^{-1} ν = 1686 (C=O); HRMS: m/z (ES) 213.0912, $C_{12}H_{14}NaO_2$, [M+Na]$^+$ requires 213.0886.

General Procedure for the Synthesis of β-Alkenyl-β-hydroxy-*N*-acyloxazolidin-2-ones:

Acylated (*S*)-4-benzyl-5,5-dimethyloxazolidin-2-one **7a** or **7b** (1 equiv.) was dissolved in dry dichloromethane at 0 ˚C under nitrogen and was stirred for 30 minutes. 9-Borabicyclo[3.3.1]nonyl trifluoromethanesulfonate (9-BBN-OTf) (1.1 equiv., 0.5 M solution in hexanes) or dibutylboron triflate (1.1 equiv., 1.0 M in dichloromethane) was added dropwise. After 30 minutes, *N,N*-diisopropylethylamine (1.3 equiv.) was added and the resulting solution was stirred for 30 minutes before the reaction was cooled to -78 ˚C. The appropriate aldehyde (1.3 equiv.) was added in one portion and the reaction was allowed to warm to ambient temperature overnight. The reaction was quenched with pH 7 buffer solution (Na_2PO_4/NaH_2PO_4) (10 mL) and was stirred for ten minutes. Hydrogen peroxide (4 mL) and methanol (8 mL) were then added and the solution was stirred for a further two hours. The methanol was evaporated, the solution diluted with dichloromethane and washed with saturated $NaHCO_3$ and brine. The combined organic extracts were dried over $MgSO_4$ and concentrated to afford crude product.

(*S*)-4-Benzyl-3-((2*S*,3*S*)-3-hydroxy-2-methyl-4-methylenehexanoyl)-5,5-dimethyloxazoli

din-2-one, 1a: The title compound was prepared according to the general procedure from 9-

BBN-OTf (9.46 mL, 4.7 mmol), (*S*)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a**

(1.08 g, 4.3 mmol), *N*,*N*-diisopropylethylamine (0.94 mL, 5.4 mmol) and ethacrolein (0.45 g,

5.4 mmol) in dichloromethane (90 mL) to afford a crude product as a pale yellow oil. The

crude product was purified using flash silica chromatography to afford (*S*)-4-benzyl-3-

((2*S*,3*S*)-3-hydroxy-2-methyl-4-methylenehexanoyl)-5,5-dimethyloxazolidin-2-one **1a** (1.19

g, 3.4 mmol, 80%) as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.34-7.20 (5H, m,

Ph), 5.16 (1H, app. t, *J* = 1.0 Hz, C*H*$_{cis}$H$_{trans}$=C), 4.98 (1H, app. t, *J* = 1.0 Hz, CH$_{cis}$*H*$_{trans}$=C),

4.53 (1H, dd, *J* = 9.0, 4.0 Hz, C*H*N), 4.40 (1H, d, *J* = 3.5 Hz, C*H*OH), 3.96 (1H, qd, *J* = 7.0,

3.5 Hz, C*H*CO), 3.08 (1H, dd, *J* = 14.0, 4.0 Hz, C*H*$_A$H$_B$Ph), 2.91 (1H, dd, *J* =14.0, 9.5 Hz,

CH$_A$*H*$_B$Ph), 2.91 (1H, br. s, OH), 2.02 (2H, m, C*H*$_2$CH$_3$) 1.40 (3H, s, (C*H*$_3$)C(CH$_3$)), 1.38

(3H, s, (CH$_3$)C(C*H*$_3$)), 1.11 (3H, d, *J* = 7.0 Hz, C*H*$_3$CH), 1.07 (3H, t, *J* = 7.0, C*H*$_3$CH$_2$);

^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 177.5, 152.6, 150.3, 137.0, 129.5, 129.1, 127.3, 109.9,

82.7, 74.1, 63.8, 41.1, 35.8, 28.8, 25.7, 22.6, 12.5, 11.1; IR cm^{-1} ν = 3497 (br. OH), 1773

(C=O$_{ox}$), 1700 (C=O); HRMS: *m/z* (ES) 346.2014, C$_{20}$H$_{28}$NO$_4$ [M+H]$^+$ requires 346.2013;

$[\alpha]_D^{21}$ = -36.0 (*c* = 1.00 g/100 mL in CHCl$_3$).

(*S*)-4-Benzyl-3-((2*S*,3*S*)-6-(benzyloxy)-3-hydroxy-2-methyl-4-methylenehexanoyl)-5,5-di

methyloxazolidin-2-one, 1b: The title compound was prepared according to the general

procedure from dibutylboron triflate (1.78 mL, 1.8 mmol), (*S*)-4-benzyl-5,5-dimethyl-3-

propionyloxazolidin-2-one **7a** (0.423 g, 1.6 mmol), *N*,*N*-diisopropylethylamine (0.36 mL, 2.1

mmol) and 4-(benzyloxy)-2-methylenebutanal (0.40 g, 2.1 mmol) in dichloromethane (5 mL)

to afford a crude product as a pale yellow oil. The crude product was purified using flash

silica chromatography [1:4 EtOAc:Petroleum ether, R$_f$ 0.27] to afford (*S*)-4-benzyl-3-

((2*S*,3*S*)-6-(benzyloxy)-3-hydroxy-2-methyl-4-methylenehexanoyl)-5,5-dimethyloxazolidin-

2-one **1b** (0.57 g, 1.3 mmol, 78%) as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.27-7.16 (10H, m, Ph, Ph$_\text{ox}$), 5.11 (1H, s, C=CH$_A$H$_B$), 4.95 (1H, s, C=CH$_A$H$_B$), 4.45-4.40 (3H, m, OCH$_2$Ph, CHN), 4.32 (1H, br. d, J = 5.8 Hz, CHOH), 4.00 (1H, app. quintet, J = 6.6 Hz, CHCH$_3$), 3.62-3.48 (2H, m, CH$_2$OBn), 3.18 (1H, br. s, OH), 2.99 (1H, dd, J = 14.4, 4.3 Hz, CH$_A$H$_B$Ph), 2.83 (1H, dd, J = 14.1, 8.7 Hz, CH$_A$H$_B$Ph), 2.44-2.35 (1H, m, CH$_A$H$_B$OBn), 2.29-2.21 (1H, m, CH$_A$H$_B$OBn), 1.31 (3H, s, C(CH$_3$)(CH$_3$)), 1.26 (3H, s, C(CH$_3$)(CH$_3$)), 1.12 (3H, d, J = 6.9 Hz, CHCH$_3$); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 176.3, 152.2, 146.8, 137.9, 136.7, 129.1, 128.6, 128.4, 127.7, 127.6, 126.8, 113.3, 82.2, 74.5, 73.0, 70.0, 63.3, 41.5, 35.3, 32.7, 28.2, 22.1, 12.0; IR cm^{-1} ν = 3467 (OH), 1770 (C=O$_\text{ox}$), 1694 (C=O); HRMS: m/z (ES) 452.2458, C$_{27}$H$_{34}$NO$_5$ [M+H]$^+$ requires 452.2436; $[\alpha]_\text{D}^{17}$ = -30.0 (c = 0.50 g/100 mL in CHCl$_3$).

(S)-4-Benzyl-3-((2S,3R)-3-hydroxy-2-methylpent-4-enoyl)-5,5-dimethyloxazolidin-2-one, 1c: The title compound was prepared according to the general procedure from 9-BBN-OTf (3.78 mL, 1.9 mmol), (S)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a** (0.40 g, 1.7 mmol), N,N-diisopropylethylamine (0.43 ml, 2.5 mmol) and acrolein (0.16 mL, 2.5 mmol) in dichloromethane (90 mL) to afford a crude product as a pale yellow oil. The crude product was purified using flash silica chromatography to afford (S)-4-benzyl-3-((2S,3R)-3-hydroxy-2-methylpent-4-enoyl)-5,5-dimethyloxazolidin-2-one **1c** (0.26 g, 0.9 mmol, 53%) as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.26-7.12 (5H, m, Ph), 5.83-5.70 (1H, ddd, J = 10.5, 5.5, 5.3 Hz, CH=CH$_2$), 5.25 (1H, dt, J = 1.5 Hz, CH$_{cis}$H$_{trans}$=C), 5.13 (1H, dt, J = 10.5, 1.5 Hz, CH$_{cis}$H$_{trans}$=C), 4.49 (1H, dd, J = 9.0, 4.5 Hz, CHN), 4.38 (1H, m, CHOH), 3.85 (1H, dq, J = 7.0, 4.0 Hz, CHCH$_3$), 3.0 (1H, dd, J = 14.5, 4.5 Hz, CH$_A$H$_B$Ph), 2.85 (1H, dd, J =14.5, 9.0 Hz, CH$_A$H$_B$Ph), 2.65 (1H, br. s, OH), 1.33 (3H, s, (CH$_3$)C(CH$_3$)), 1.31 (3H, s, (CH$_3$)C(CH$_3$)), 1.10 (3H, d, J = 7.0 Hz, CH$_3$CH); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 176.9 152.8, 137.7, 137.0, 129.5, 129.1, 127.3, 116.8, 82.8, 73.2, 63.8, 42.85, 35.9, 28.8, 22.6, 11.7;

IR cm^{-1} ν = 3501 (br. OH), 1754 (C=O), 1702 (C=O$_{ox}$); HRMS: m/z (ES) 340.1577, C$_{18}$H$_{23}$NNaO$_4$ [M+Na]$^+$ requires 340.1519; $[\alpha]_D^{22}$ = -26.0 (c = 0.60 g/100 mL in CHCl$_3$).

(S)-4-Benzyl-3-((2S,3R,E)-3-hydroxy-2-methyl-5-phenylpent-4-enoyl)-5,5-dimethyloxazolidin-2-one, 1d: The title compound was prepared according to the general procedure from 9-BBN-OTf (10.10 mL, 5.0 mmol), (S)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a** (1.20 g, 4.6 mmol), N,N-diisopropylethylamine (1.03 mL, 5.9 mmol) and (E)-cinnimaldehyde (0.76 mL, 5.9 mmol) in dichloromethane (30 mL) to afford a crude product as a pale yellow oil. The crude product was purified using flash silica chromatography to afford (S)-4-benzyl-3-((2S,3R,E)-3-hydroxy-2-methyl-5-phenylpent-4-enoyl)-5,5- dimethyloxazolidin-2-one **1d** (1.41 g, 3.6 mmol, 78%) as a colourless oil. mp = 147–149 °C (Et$_2$O); ^{1}H NMR (300 MHz, CDCl$_3$): δ$_H$ 7.36-7.13 (10H, m, Ph), 6.59 (1H, dd, J = 16.0, 1.5 Hz, CH=CHPh), 6.12 (1H, dd, J = 16.0 Hz, 6.0 Hz, CH=CHPh), 4.54 (1H, m, CHOH), 4.47 (1H, dd, J = 9.0, 5.0 Hz, CHN), 3.94 (1H, qd, J = 7.0, 4.0 Hz, COCH), 3.00 (1H, dd J = 14.0, 5.0 Hz, CH$_A$H$_B$Ph), 2.84 (1H, dd, J = 14.0, 9.0 Hz, CH$_A$CH$_B$Ph), 2.74 (1H, br. s, OH), 1.32 (3H, s, (CH$_3$)C(CH$_3$)), 1.30 (3H, s, (CH$_3$)C(CH$_3$)), 1.13 (3H, d, J = 7.0 Hz, CH$_3$CH); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ$_C$ 177.1, 152.6, 137.7, 134.1, 129.3, 129.2, 129.1, 127.3, 82.7, 73.4, 63.8, 43.3, 35.9, 32.7, 32.2, 29.6, 29.5, 23.1, 14.5, 12.0; IR cm^{-1} ν = 3443 (OH), 1768 (C=O), 1684 (C=O$_{ox}$); HRMS: m/z (ES) 416.1821, C$_{24}$H$_{27}$NNaO$_4$ [M+Na]$^+$ requires 416.1838; $[\alpha]_D^{23}$ = +6.0 (c = 0.89 g/100 mL in CHCl$_3$).

(S)-4-Benzyl-3-((2S,3R,E)-3-hydroxy-2-methylhex-4-enoyl)-5,5-dimethyl-oxazolidin-2-one, 1e: The title compound was prepared according to the general procedure from 9-BBN-OTf (5.56 mL, 2.8 mmol), (S)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a** (0.61 g, 2.3 mmol), N,N-diisopropylethylamine (0.53 ml, 3.0 mmol) and (E)-crotonaldehyde (0.25 mL, 3.0 mmol) in dichloromethane (50 mL) to afford a crude product as a pale yellow oil.

The crude product was purified using flash silica chromatography to afford (S)-4-benzyl-3-((2S,3R,E)-3-hydroxy-2-methylhex-4-enoyl)-5,5-dimethyloxazolidin-2-one **1e** (0.70 g, 2.1 mmol, 91%) as a clear oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.39-7.17 (5H, m, Ph), 5.74 (1H, dqd, J = 15.5, 6.5, 1.0 Hz, CH=CHCH$_3$), 5.48 (1H, ddd, J = 15.5, 6.5, 1.0 Hz, CH=CHCH$_3$), 4.60 (1H, dd, J = 9.0, 4.5 Hz, CHN), 4.53 (1H, m, CHOH), 3.91 (1H, qd, J = 7.0, 4.5 Hz, COCH), 3.05 (1H, dd J =14.5, 4.5 Hz, CH$_A$H$_B$Ph), 2.90 (1H, dd. J = 14.5, 9.0 Hz, CH$_A$H$_B$Ph), 2.60 (1H, d, J = 2.5 Hz, OH), 1.70 (3H, d, J = 7.0 Hz, CH$_3$CH=CH), 1.39 (3H, s, (CH$_3$)C(CH$_3$)), 1.38 (3H, s, (CH$_3$)C(CH$_3$)), 1.15 (3H, d, J = 7.0 Hz, CH$_3$CH); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 176.9, 152.9, 137.1, 130.5, 129.5, 129.1, 128.9, 127.3, 82.7, 73.6, 63.8, 43.2, 35.9, 28.7, 22.5, 18.2, 12.1; IR cm^{-1} ν = 3508 (br. OH), 1775 (C=O$_{ox}$), 1696 (C=O); HRMS: m/z (ES) 332.1855, C$_{19}$H$_{26}$NO$_4$ [M+H]$^+$ requires 332.1856; $[\alpha]_D^{21}$ = -14.0 (c = 0.84 g/100 mL in CHCl$_3$).

(S)-4-Benzyl-3-((2S,3R,E)-6-(benzyloxy)-3-hydroxy-2-methylhex-4-enoyl)-5,5-dimethyl oxazolidin-2-one, 1f: Based on a literature procedure,[27] (S)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a** (1.95 g, 7.5 mmol) was dissolved in dry dichloromethane (50 mL) at -10 ˚C under nitrogen and was stirred for 20 minutes. Dibutylboron triflate (8.97 mL, 9.0 mmol, 1.0 M in dichloromethane) was added dropwise followed by triethylamine (1.35 mL, 9.7 mmol) and the resulting solution was stirred for 30 minutes at 0 ˚C. The reaction was cooled to -78 ˚C and (E)-4-(benzyloxy)but-2-enal (1.45 g, 8.2 mmol) was added dropwise. The solution was stirred at -78 ˚C for 45 minutes and then warmed to 0 ˚C and stirred for a further 3 hours. The reaction was cooled to -10 ˚C and pH 7 buffer solution (Na$_2$PO$_4$/NaH$_2$PO$_4$) (30 mL) was added followed by methanol (24 mL) and hydrogen peroxide (12 mL). The methanol was evaporated, the solution diluted with dichloromethane and washed with saturated NaHCO$_3$ and brine. The combined organic extracts were dried over MgSO$_4$ and concentrated. The crude product was purified using flash silica

chromatography [1:4 EtOAc:Petroleum ether, R_f 0.19] to afford (*S*)-4-benzyl-3-((2*S*,3*R*,*E*)-6-(benzyloxy)-3-hydroxy-2-methylhex-4-enoyl)-5,5-dimethyloxazolidin-2-one **1f** (2.91 g, 6.7 mmol, 89%) as a yellow oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.27-7.15 (10H, m, Ph, Ph$_{ox}$), 5.83 (1H, dtd, *J* = 15.6, 5.4, 1.0 Hz, CH=C*H*CH$_2$OBn), 5.68 (1H, dd, *J* = 15.6, 5.4 Hz, C*H*=CHCH$_2$OBn), 4.48-4.38 (4H, m, C*H*$_2$OBn, C*H*N, C*H*OH), 3.96 (2H, d, *J* = 5.4 Hz, C*H*$_2$OBn), 3.86 (1H, qd, *J* = 7.0, 4.2 Hz, C*H*CH$_3$), 2.99 (1H, dd, *J* = 14.2, 4.6 Hz, C*H*$_A$H$_B$Ph), 2.82 (1H, dd, *J* = 14.4, 9.0 Hz, CH$_A$*H*$_B$Ph), 2.76 (1H, broad s, O*H*), 1.30 (3H, s, C(C*H*$_3$)(CH$_3$)), 1.28 (3H, s, C(CH$_3$)(C*H*$_3$)), 1.10 (3H, d, *J* = 7.1 Hz, CHC*H*$_3$); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 176.3, 152.4, 138.2, 136.6, 132.0, 129.1, 128.7, 128.6, 128.3, 127.7, 127.6, 126.8, 82.3, 72.2, 72.1, 70.0, 63.3, 42.7, 35.4, 28.3, 22.1, 11.6; IR cm^{-1} ν = 3474 (OH), 1771 (C=O$_{ox}$), 1693 (C=O); HRMS: *m/z* (ES) 460.2064, C$_{26}$H$_{31}$NNaO$_5$ [M+Na]$^+$ requires 460.2099; $[\alpha]_D^{25}$ = -28.0 (*c* = 0.50 g/100 mL in CHCl$_3$).

(*S*)-4-Benzyl-3-((2*S*,3*R*,*Z*)-6-(benzyloxy)-3-hydroxy-2-methylhex-4-enoyl)-5,5-dimethyl oxazolidin-2-one, 1g: Based on a literature procedure,[27] (*S*)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a** (0.50 g, 1.9 mmol) was dissolved in dry dichloromethane (20 mL) at -10 °C under nitrogen and was stirred for 20 minutes. Dibutylboron triflate (2.29 mL, 2.3 mmol, 1.0 M in dichloromethane) was added dropwise followed by triethylamine (0.35 mL, 2.5 mmol) and the resulting solution was stirred for 30 minutes at 0 °C. The reaction was cooled to -78 °C and (*Z*)-4-(benzyloxy)but-2-enal (0.37 g, 2.1 mmol) was added dropwise. The solution was stirred at -78 °C for 45 minutes and then warmed to 0 °C and stirred for a further three hours. The reaction was cooled to -10 °C and pH 7 buffer solution (Na$_2$PO$_4$/NaH$_2$PO$_4$) (10 mL) was added followed by methanol (8 mL) and hydrogen peroxide (4 mL). The methanol was evaporated, the solution diluted with dichloromethane and washed with saturated NaHCO$_3$ and brine. The combined organic extracts were dried over MgSO$_4$ and concentrated. The crude product was purified using flash silica chromatography [1:2

EtOAc:Petroleum ether, R$_f$ 0.63] to afford (*S*)-4-benzyl-3-((2*S*,3*R*,*Z*)-6-(benzyloxy)-3-hydroxy-2-methylhex-4-enoyl)-5,5-dimethyloxazolidin-2-one **1g** (0.74 g, 1.7 mmol, 88%) as a colourless gum, which crystallised on standing. ^{1}H NMR (300 MHz, CDCl$_3$): δ$_H$ 7.29-7.12 (10H, m, Ph), 5.71-5.52 (2H, m, C*H*=C*H*), 4.63-4.49 (1H, m, C*H*OH), 4.44-4.39 (3H, m, C*H*$_2$OBn, C*H*N), 4.10 (1H, ddd, *J* = 12.7, 6.5, 1.3 Hz, C*H*$_A$H$_B$OBn), 4.00 (1H, ddd, *J* = 12.6, 5.5, 1.3 Hz, CH$_A$*H*$_B$OBn), 3.87 (1H, m, C*H*CH$_3$), 2.97 (1H, dd, *J* = 14.3, 4.5 Hz, C*H*$_A$H$_B$Ph), 2.81 (1H, dd, *J* = 14.3, 9.0 Hz, CH$_A$*H*$_B$Ph), 2.73 (1H, broad s, O*H*), 1.30 (3H, s, C(C*H*$_3$)(CH$_3$)), 1.26 (3H, s, C(CH$_3$)(C*H*$_3$)), 1.11 (3H, d, *J* = 7.0 Hz, CHC*H*$_3$); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ$_C$ 175.9, 152.6, 138.1, 136.7, 132.1, 129.6, 129.2, 128.7, 128.5, 127.9, 127.8, 126.9, 82.4, 72.5, 69.0, 66.2, 63.4, 43.1, 35.5, 28.4, 22.2. 12.4; IR cm^{-1} ν = 3477 (OH), 1771 (C=O$_{ox}$), 1692 (C=O); HRMS: *m/z* (ES) 460.2097, C$_{26}$H$_{31}$NNaO$_5$ [M+Na]$^+$ requires 460.2099; $[\alpha]_D^{25}$ = -12.0 (*c* = 0.50 g/100 mL in CHCl$_3$).

(*S*)-4-Benzyl-3-((2*S*,3*S*,*E*)-3-hydroxy-2,4-dimethylhept-4-enoyl)-5,5-dimethyloxazolidin-2-one, 1h: The title compound was prepared according to the general procedure from 9-BBN-OTf (7.08 mL, 3.5 mmol), (*S*)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a** (0.84 g, 3.2 mmol), *N*,*N*-diisopropylethylamine (0.73 mL, 4.2 mmol) and 2-methyl-pentenal (0.48 mL, 4.2 mmol) in dichloromethane (100 mL) to afford a crude product as a pale yellow oil. The crude product was purified using flash silica chromatography to afford (*S*)-4-benzyl-3-((2*S*,3*S*,*E*)-3-hydroxy-2,4-dimethylhept-4-enoyl)-5,5-dimethyloxazolidin-2-one **1h** (0.95 g, 2.6 mmol, 82%) as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ$_H$ 7.27-7.12 (5H, m, Ph), 6.51 (1H, tt, *J* = 7.0, 1.5 Hz, C=C*H*), 4.45 (1H, dd, *J* = 9.0, 4.5 Hz, C*H*N), 4.23 (1H, br. s, C*H*OH), 3.91 (1H, dq, *J* = 7.0, 4.0 Hz, COC*H*), 3.10 (1H, dd *J* = 14.5, 4.5 Hz, C*H*$_A$CH$_B$Ph), 2.84 (1H, dd, *J* = 14.5, 9.0 Hz, CH$_A$C*H*$_B$Ph), 2.84 (1H, br. d, OH), 2.10 − 1.92 (2H, m, C*H*$_2$CH$_3$), 1.53 (3H, s, C*H*$_3$C=CH), 1.32 (3H, s, (C*H*$_3$)C(CH$_3$)), 1.29 (3H, s, (CH$_3$)C(C*H*$_3$)), 1.00 (3H, d, *J* = 7.0 Hz, C*H*$_3$CH), 0.90 (3H, t, *J* = 7.5 Hz, CH$_2$C*H*$_3$); ^{13}C{^{1}H} NMR (75 MHz,

CDCl$_3$): δ_C 177.3, 152.7, 137.1, 133.4, 129.5, 129.0, 128.8, 127.2, 82.67, 76.1, 63.8, 41.1, 35.8, 28.7, 22.5, 21.3, 14.4, 13.5, 11.5; IR cm^{-1} ν = 3493 (br. OH), 1777 (C=O), 1680 (C=O); HRMS: m/z (ES) 382.1977, C$_{21}$H$_{29}$NNaO$_4$ [M+Na]$^+$ requires 382.1994; $[\alpha]_D^{25}$ = -5.0 (c = 1.00 g/100 mL, CHCl$_3$).

(S)-4-Benzyl-3-((2S,3S,E)-6-(benzyloxy)-3-hydroxy-2,4-dimethylhex-4-enoyl)-5,5-dimethyloxazolidin-2-one, 1i: The title compound was prepared according to the general procedure from dibutylboron triflate (1.50 mL, 1.5 mmol), (S)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a** (0.36 g, 1.4 mmol), N,N-diisopropylethylamine (0.31 mL, 1.8 mmol) and (E)-4-(benzyloxy)-2-methylbut-2-enal[28] (0.34 g, 1.8 mmol) in dichloromethane (3 mL) to afford a crude product as a pale yellow oil. The crude product was purified using flash silica chromatography [1:9 EtOAc:Petroleum ether, R$_f$ 0.24] to afford (S)-4-benzyl-3-((2S,3S,E)-6-(benzyloxy)-3-hydroxy-2,4-dimethylhex-4-enoyl)-5,5-dimethyloxazolidin-2-one **1i** (0.28 g, 0.6 mmol, 46%) as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.27-7.15 (10H, m, Ph, Ph$_{ox}$), 5.71 (1H, br. t, J = 6.3 Hz, C=CH), 4.46-4.43 (3H, m, OCH_2Ph, CHN), 4.28 (1H, d, J = 3.7 Hz, CHOH), 4.02 (2H, d, J = 6.6 Hz, CH_2OBn), 3.96-3.91 (1H, m, CHCH$_3$), 3.01 (1H, dd, J = 14.3, 4.0 Hz, CH_AH$_B$Ph), 2.82 (2H, dd, broad s, J = 14.3, 9.1 Hz, CH$_A$$H_BPh, OH$), 1.57 (3H, s, C$H_3$C=CH), 1.30 (3H, s, C(C$H_3$)(CH$_3$)), 1.26 (3H, s, C(CH$_3$)(C$H_3$)), 1.05 (3H, d, J = 7.4 Hz, CHCH_3); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 176.6, 152.3, 138.3, 138.1, 136.7, 129.1, 128.6, 128.4, 127.8, 127.6, 126.9, 122.9, 82.4, 75.2, 72.1, 66.2, 63.5, 40.6, 35.3, 28.3, 22.1, 13.6, 10.9; IR cm^{-1} ν = 3481 (OH), 1771 (C=O$_{ox}$), 1698 (C=O); HRMS: m/z (ES) 452.2446, C$_{27}$H$_{34}$NO$_5$ [M+H]$^+$ requires 452.2436; $[\alpha]_D^{20}$ = -42.0 (c = 0.50 g/100 mL in CHCl$_3$).

(S)-4-Benzyl-3-((2S,3R)-3-hydroxy-2,5-dimethylhex-4-enoyl)-5,5-dimethyloxazolidin-2-one, 1j: The title compound was prepared according to the general procedure from 9-BBN-

OTf (8.05 mL, 4.0 mmol), (*S*)-4-benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one **7a** (0.96 mg, 3.7 mmol), *N,N*-diisopropylethylamine (0.83 ml, 4.8 mmol) and 3-methyl-2-butenal (0.46 mL, 4.8 mmol) in dichloromethane (100 mL) to afford a crude product as a pale yellow oil. The crude product was purified using flash silica chromatography to afford (*S*)-4-benzyl-3-((2*S*,3*R*)-3-hydroxy-2,5-dimethylhex-4-enoyl)-5,5-dimethyloxazolidin-2- one **1j** (1.28 g, 3.7 mmol, 92%) as a white solid. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.35-7.17 (5H, m, Ph), 5.23 (1H, d, *J* = 9.0 Hz, C*H*C=C), 4.60 (1H, m, C*H*OH), 4.52 (1H, dd, *J* = 9.0, 4.5 Hz, C*H*N), 3.93 (1H, qd, *J* = 7.0, 5.0 Hz, COC*H*), 3.05 (1H, dd *J* = 14.5, 4.5 Hz, C*H*$_A$CH$_B$Ph), 2.90 (1H, dd, *J* = 14.5, 9.0 Hz, CH$_A$C*H*$_B$Ph), 2.35 (1H, br. s, OH), 1.72 (3H, s, C=C(C*H*$_3$)$_A$(CH$_3$)$_B$), 1.68 (3H, s, C=C(CH$_3$)$_A$(C*H*$_3$)$_B$), 1.39 (3H, s, (C*H*$_3$)C(CH$_3$)), 1.37 (3H, s, (CH$_3$)C(C*H*$_3$)), 1.18 (3H, d, *J* = 7.0 Hz, C*H*$_3$CH); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 176.7, 153.0, 137.2, 137.1, 129.5, 129.1, 127.3, 124.5, 82.6, 69.9, 63.8, 43.4, 35.9, 28.6, 26.4, 22.5, 18.8, 12.6; IR cm^{-1} ν = 3479 (br. OH), 1769 (C=O), 1681 (C=O); HRMS: *m/z* (ES) 346.2011, C$_{20}$H$_{28}$NO$_4$ [M+H]$^+$ requires 346.2013; $[\alpha]_D^{21}$ = -27.0 (*c* = 1.00 g/100 mL in CHCl$_3$).

(*S*)-4-Benzyl-3-((2*S*,3*S*)-3-hydroxy-4-methyl-2-phenylpent-4-enoyl)-5,5-dimethyloxazolidin-2-one, 1k: The title compound was prepared according to the general procedure from 9-BBN-OTf (0.45 mL, 0.9 mmol), (*S*)-4-benzyl-5,5-dimethyl-3-(2-phenylacetyl)oxazolidin-2-one **7b** (0.27 g, 0.8 mmol), *N,N*-diisopropylethylamine (0.17 ml, 1.0 mmol) and methacrolein (0.08 mL, 1.0 mmol) in dichloromethane (70 mL) to afford a crude product as a pale yellow oil. The crude product was purified using flash silica chromatography to afford (*S*)-4-benzyl-3-((2*S*,3*S*)-3-hydroxy-4-methyl-2-phenylpent-4-enoyl)-5,5-dimethyloxazolidin-2-one **1k** (0.24 g, 0.6 mmol, 75%) as a colourless oil. ^{1}H NMR (300 MHz,CDCl$_3$): δ_H 7.42-7.20 (5H, m, Ph), 7.14-6.98 (5H, m, Ph), 5.27 (1H, d, *J* = 7.0 Hz, PhC*H*) 4.92 (1H, m, C*H*$_{cis}$H$_{trans}$=C), 4.85 (1H, br. app. pent., *J* = 1.5 Hz, CH$_{cis}$*H*$_{trans}$=C), 4.69 (1H, d, *J* = 8.0 Hz, C*H*OH), 4.43 (1H, dd, *J* = 9.0, 4.0 Hz, C*H*N), 2.82 (1H, dd *J* = 14.0, 4.0 Hz, C*H*$_A$H$_B$Ph), 2.63 (1H, dd, *J* =

14.0, 9.0 Hz, CH$_A$CH$_B$Ph), 2.05 (1H, br. s, OH), 1.74 (3H, s, CH$_2$=CCH$_3$), 1.27 (3H, s, (CH$_3$)C(CH$_3$)), 1.24 (3H, s, (CH$_3$)C(CH$_3$)); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 172.9, 152.5, 144.8, 136.9, 134.7, 130.26, 129.4, 129.1, 128.9, 128.4, 127.1, 114.2, 82.5, 63.7, 53.4, 35.3, 28.7, 22.5, 18.7; IR cm^{-1} ν = 3489 (OH), 1768 (C=O), 1671 (C=O$_{ox}$); HRMS: m/z (ES) 394.2019, C$_{24}$H$_{28}$NO$_4$ [M+H]$^+$ requires 394.2018; $[\alpha]_D^{25}$ = -89.9 (c = 1.00 g/100 mL, CHCl$_3$).

General Procedure for the Synthesis of (3S,4S)-Hydroxy-γ-lactones (6a-6k, 11): Osmium tetroxide (OsO$_4$) (0.1 equiv.) was added in one portion to a stirring solution of the appropriate β-alkenyl-β-hydroxy-N-acyloxazolidin-2-one **1a-1k** (1.0 equiv.) in acetone/water (8:1 ratio) under nitrogen. After five minutes, NMO (N-methylmorpholine N-oxide, 60% by weight in water, 1.1 equiv.) was added in one portion and stirred for 24 hours. The resulting reaction mixture was concentrated under reduced pressure and immediately purified *via* column chromatography.

(3S,4S,5R)-5-Ethyl-4-hydroxy-5-(hydroxymethyl)-3-methyldihydrofuran-2(3H)-one, 6a: OsO$_4$ (22 mg, 0.09 mmol) was added to a solution of **1a** (305 mg, 0.88 mmol) in acetone/water (8:1, 3 mL) followed by addition of NMO (60% by weight in water, 0.16 mL, 0.97 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded **6a** (120 mg, 0.61 mmol, 69 %, 49:1 dr). ^{1}H NMR (500 MHz, MeOD): δ_H 4.24 (1H, d, J = 9.4 Hz, CHOH), 3.74 (1H, d, J = 12.1 Hz, CH$_A$H$_B$OH), 3.52 (1H, d, J = 12.2 Hz, CH$_A$H$_B$OH), 2.68 (1H, qd, J = 9.4, 7.1 Hz, CHCO), 1.81 (1H, dq, J = 15.0, 7.5 Hz, CH$_A$H$_B$CH$_3$), 1.71 (1H, dq, J = 15.0 , 7.5 Hz, CH$_A$H$_B$CH$_3$), 1.28 (3H, d, J = 7.5 Hz, CH$_3$), 1.01 (3H, t, J = 7.5 Hz, CH$_2$CH$_3$); ^{13}C{^{1}H} NMR (75 MHz, MeOD): δ_C 179.6, 90.2, 76.5, 64.7, 44.2, 25.0, 13.9, 8.6; IR cm^{-1} ν = 3368 (br. OH), 1751 (C=O); HRMS: m/z (ES) 175.0957, C$_8$H$_{15}$O$_4$ [M+H]$^+$ requires 175.0970; $[\alpha]_D^{24}$ = - 3.4 (c = 0.88 g/100 mL in CHCl$_3$).

(3*S*,4*S*,5*R*)-5-(2-(Benzyloxy)ethyl)-4-hydroxy-5-(hydroxymethyl)-3-methyldihydrofuran-2(3H)-one, 6b: OsO_4 (8 mg, 0.03 mmol) was added to a solution of **1b** (140 mg, 0.31 mmol) in acetone/water (8:1, 1.5 mL) followed by addition of NMO (60% by weight in water, 0.07 mL, 0.34 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded **6b** (80 mg, 0.28 mmol, 93%, 10:1 dr). ^1H NMR (300 MHz, $CDCl_3$): δ_H 7.31-7.18 (5H, m, Ph), 4.43 (2H, s, OC*H$_2$*Ph), 4.12 (1H, br. s, O*H*), 3.96 (1H, d, *J* = 8.4 Hz, C*H*OH), 3.59-3.49 (4H, m, C*H$_2$*OBn, C*H$_2$*OH), 2.80 (1H, br. s, OH), 2.49 (1H, app. quintet, *J* = 7.4 Hz, C*H*CH$_3$), 2.07-1.91 (2H, m, C*H$_2$*CH$_2$OBn), 1.20 (3H, d, *J* = 7.4 Hz, CHC*H$_3$*); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ_C 177.4, 136.5, 128.8, 128.5, 128.3, 87.8, 76.5, 73.9, 66.4, 64.8, 42.9, 30.3, 13.7; IR cm^{-1} ν = 3402 (OH), 1754 (C=O); HRMS: *m/z* (ES) 303.1210, $C_{15}H_{20}NaO_5$, $[M+Na]^+$ requires 303.1208; $[\alpha]_D^{24}$ = +18.0 (*c* = 0.50 g/100 mL in $CHCl_3$).

(3*S*,4*S*,5*R*)-4-Hydroxy-5-(hydroxymethyl)-3-methyldihydrofuran-2(3*H*)-one, 6c: OsO_4 (15 mg, 0.06 mmol) was added to a solution of **1c** (150 mg, 0.52 mmol) in acetone/water (8:1, 5 mL) followed by addition of NMO (60% by weight in water, 0.09 mL, 0.52 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded a diastereomeric mixture of **6c major** and **6c minor** (60 mg, 0.41 mmol, 79%, 3:1 dr). The two diastereoisomers were analysed as a mixture. **(3*S*,4*S*,5*R*)-major:** ^1H NMR (500 MHz, MeOD): δ_H 4.19-4.17 (1H, m, C*H*CH$_2$OH), 4.02 – 3.99 (1H, m, C*H*OH), 3.94 (1H, dd, *J* = 12.8, 2.5 Hz, C*H$_A$*CH$_B$OH), 3.72 (1H, dd, *J* = 12.8, 4.8 Hz, CH$_A$C*H$_B$*OH), 2.66 (1H, dq, *J* = 8.9, 7.1 Hz, C*H*CH$_3$), 1.30 (3H, d, *J* = 7.3 Hz, C*H$_3$*); $^{13}C\{^1H\}$ NMR (75 MHz, MeOD): δ_C 180.0, 86.8, 75.6, 62.0, 45.7, 13.6; **(3*S*,4*S*,5*S*)-minor:** ^1H NMR (500 MHz, $CDCl_3$): δ_H 4.57 (1H, dt, *J* = 5.8, 3.7 Hz, C*H*CH$_2$OH), 4.27 (1H, t, *J* = 6.0 Hz, C*H*OH), 3.90 (2H, d, *J* = 3.7 Hz, C*H$_A$*C*H$_B$*OH), 2.71 (1H, dt, *J* = 13.6, 7.6 Hz, C*H*CH$_3$), 1.29 (3H, d, *J* = 7.5 Hz, C*H$_3$*); $^{13}C\{^1H\}$ NMR (75 MHz, MeOD): δ_C 181.6, 84.1,

76.2, 62.2, 45.5, 14.4; IR cm^{-1} ν = 3377 (br. OH), 2934 (br. OH), 1763 (C=O); HRMS: *m/z* (ES) 147.0650, C$_6$H$_{11}$O$_4$ [M+H]$^+$ requires 147.0657; $[\alpha]_D^{24}$ = +4.0 (*c* = 0.50 g/100 mL in MeOH).

(3*S*,4*S*,5*S*)-4-Hydroxy-5-((*S*)-hydroxy(phenyl)methyl)-3-methyldihydrofuran-2(3*H*)-one, 6d: OsO$_4$ (13 mg, 0.05 mmol) was added to a solution of **1d** (198 mg, 0.50 mmol) in acetone/water (8:1, 3 mL) followed by addition of NMO (60% by weight in water, 0.1 mL, 0.55 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded **6d** (90 mg, 0.41 mmol, 81 %, 9:1 dr). ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$ 7.41-7.25 (5H, m, Ph), 4.76 (1H, d, *J* = 5.7, C*H*Ph), 4.22 (1H, dd, *J* = 9.2, 7.5 Hz, C*H*CHPh), 3.95 (1H, dd, *J* = 9.2, 7.5 Hz, C*H*OH), 2.56 (1H, dq, *J* = 9.2, 7.2 Hz, C*H*CO), 1.19 (3H, d, *J* = 6.9 Hz, C*H$_3$*CH); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ$_C$ 178.4, 134.5, 129.1, 128.7, 127.4, 80.1, 74.9, 70.9, 43.1, 14.1; IR cm^{-1} ν = 3358 (br. OH), 1753 (C=O); HRMS: *m/z* (ES) 223.0964, C$_{12}$H$_{15}$O$_4$ [M+H]$^+$ requires 223.0970; $[\alpha]_D^{23}$ = +44.0 (*c* = 1.62 g/100 mL in CHCl$_3$).

(3*S*,4*S*,5*R*)-4-Hydroxy-5-((*S*)-1-hydroxyethyl)-3-methyldihydrofuran-2(3*H*)-one, 6e: OsO$_4$ (13 mg, 0.05 mmol) was added to a solution of **1e** (164 mg, 0.50 mmol) in acetone/water (8:1, 3 mL) followed by addition of NMO (60% by weight in water, 0.09 mL, 0.54 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded a diastereomeric mixture of **6e major** and **6e minor** (66 mg, 0.41 mmol, 83%, 5:1 dr). The two diastereoisomers were analysed as a mixture. **(3*S*,4*S*,5*R*)-major:** ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$ 4.11 (1H, dd, *J* = 8.8, 7.0 Hz, C*H*OH), 4.04-3.95 (2H, m, C*H*OCO, C*H*OHCH$_3$), 2.68 (1H, dq, *J* = 9.1, 7.1 Hz, C*H*CO), 1.37 (3H, d, *J* = 6.5 Hz, C*H$_3$*CHOH), 1.32 (3H, d, *J* = 7.1 Hz, C*H$_3$*CH); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ$_C$ 176.8, 86.4, 74.9, 66.6, 44.2, 19.9, 12.8; **(3*S*,4*S*,5*S*)-minor:** ^{1}H NMR (500

MHz, CDCl$_3$) δ_H 4.35-4.32 (1H, m, CHOH), 4.32 – 4.27 (2H, m, CHOCO, CHOHCH$_3$), 2.76 (1H, dq, J = 7.7, 5.3 Hz, CHCO), 1.39 (3H, d, J = 6.7 Hz, CH_3CHOH), 1.32 (3H, d, J = 7.5 Hz, CH_3CH); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) δ_C 177.3, 82.9, 76.3, 67.1, 44.6, 19.8, 14.0; IR cm^{-1} ν = 3356 (br. OH), 1754 (C=O); HRMS: m/z (ES) 183.0613, C$_7$H$_{12}$NaO$_4$ [M+Na]$^+$ requires 183.0628.

(3S,4S,5S)-5-((S)-2-(Benzyloxy)-1-hydroxyethyl)-4-hydroxy-3-methyldihydrofuran-2(3H)-one, 6f: OsO$_4$ (6 mg, 0.02 mmol) was added to a solution of **1f** (100 mg, 0.22 mmol) in acetone/water (8:1, 1.2 mL) followed by addition of NMO (60% by weight in water, 0.04 mL, 0.25 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded **6f** (47 mg, 0.17 mmol, 77%, 4:1 dr). ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.33-7.20 (5H, m, Ph), 4.50 (2H, s, OCH_2Ph), 4.04-3.90 (3H, m, CH$_3$CHCHOH, COOCH, OCH$_2$CHOH), 3.63-3.52 (3H, m, CH_2OBn, OH), 2.95 (1H, d, J = 4.3 Hz, OH), 2.61-2.51 (1H, m, CHCH$_3$), 1.22 (3H, d, J = 7.0 Hz, CHCH_3); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 176.6, 137.1, 128.8, 128.4, 128.1, 84.3, 74.6, 74.0, 71.1, 69.3, 43.2, 12.4; IR cm^{-1} ν = 3396 (OH), 1760 (C=O); HRMS: m/z (ES) 289.1041, C$_{14}$H$_{18}$NaO$_5$, [M+Na]$^+$ requires 289.1051; $[\alpha]_D^{24}$ = +4.0 (c = 0.50 g/100 mL in CHCl$_3$).

(3S,4S,5S)-5-((R)-2-(Benzyloxy)-1-hydroxyethyl)-4-hydroxy-3-methyldihydrofuran-2(3H)-one, 6g: OsO$_4$ (6 mg, 0.02 mmol) was added to a solution of **1g** (100 mg, 0.22 mmol) in acetone/water (8:1, 1.2 mL) followed by addition of NMO (60% by weight in water, 0.04 mL, 0.25 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded the product in 74% yield, 2:1 dr, **6g major** (28 mg, 0.11 mmol, 45%), **6g minor** (13 mg, 0.05 mmol, 21%) and a mixture of **6g major** and **6g minor** (4 mg, 0.15 mmol, 7%). **(3S,4S,5R)-5-(S)-major:** ^{1}H NMR (300 MHz, 50:50 CDCl$_3$:C$_6$H$_6$): δ_H 7.32-21 (5H, m, Ph), 4.43 (1H, d, J = 11.6 Hz, OCH_AH$_B$Ph), 4.36 (1H, d, J

= 11.6 Hz, OCH$_A$H$_B$Ph), 4.03 (1H, dd, J = 9.9, 7.3 Hz, CH$_3$CHCHOH), 3.85 (1H, dd, J = 7.3, 5.1 Hz, COOCH), 3.79-3.75 (1H, m, OCH$_2$CHOH), 3.51 (1H, dd, J = 10.3, 3.3 Hz, CH_A-H$_B$OBn), 3.46 (1H, dd, 10.3, 4.2 Hz, CH$_A$$H_B$OBn), 3.21 (1H, br. s, O$H$), 2.59 (1H, br. s, O$H$), 2.50 (1H, dq, 9.9, 7.1 Hz, CHCH$_3$), 1.25 (3H, d, J = 7.1 Hz, CHCH_3); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 176.5, 136.9, 128.8, 128.5, 128.2, 83.1, 74.5, 74.3, 70.9, 70.4, 42.7, 12.6; IR cm^{-1} ν = 3418.67 (OH), 1759.65 (C=O); HRMS: m/z (ES) 289.1042, C$_{14}$H$_{18}$NaO$_5$, [M+Na]$^+$ requires 289.1051; $[\alpha]_D^{24}$ = -2.0 (c = 0.50 g/100 mL in CHCl$_3$). **(3S,4S,5S)-5-(R)-minor:** ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.40-7.30 (5H, m, Ph), 4.59 (2H, s, OCH_2Ph), 4.43 (1H, dd, J = 8.0, 4.7 Hz, COOCH), 4.32 (1H, dd, J = 4.7, 2.6 Hz, CH$_3$CHCHOH), 4.18-4.13 (1H, m, OCH$_2$CHOH), 3.79 (1H, dd, J = 9.9, 3.3 Hz, CH_AH$_B$OBn), 3.69 (1H, dd, J = 9.9, 5.0 Hz, CH$_A$$H_B$OBn), 3.11 (1H, br. s, O$H$), 2.87 (1H, br. s, O$H$), 2.68 (1H, qd, J = 7.8, 2.5 Hz, CHCH$_3$), 1.30 (3H, d, J = 7.8 Hz, CHCH_3); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 178.4, 137.3, 128.8, 128.3, 128.1, 79.2, 75.0, 73.9, 71.0, 69.1, 43.8, 13.8; IR cm^{-1} ν = 3421 (OH), 1774 (C=O); HRMS: m/z (ES) 289.1032, C$_{14}$H$_{18}$NaO$_5$, [M+Na]$^+$ requires 289.1051; $[\alpha]_D^{24}$ = -6.0 (c = 0.50 g/100 mL in CHCl$_3$).

(3S,4S,5R)-4-Hydroxy-5-((S)-1-hydroxypropyl)-3,5-dimethyldihydrofuran-2(3H)-one, 6h: OsO$_4$ (15 mg, 0.06 mmol) was added to a solution of **1h** (209 mg, 0.58 mmol) in acetone/water (8:1, 3 mL) followed by addition of NMO (60% by weight in water, 0.11 mL, 0.64 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded (3S,4S,5R)-4-hydroxy-5-((R)-1-hydroxypropyl)-3,5-dimethyl-dihydrofuran-2(3H)-one, **6h** (89 mg, 0.48 mmol, 82%, >49:1 dr). ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 4.12 (1H, dd, J = 9.8, 5.4 Hz, CHOH), 3.93 (1H, d, J = 5.4 Hz, OH), 3.57 (1H, d, J = 8.5 Hz, OH), 3.37 (1H, ddd, J = 10.8, 8.8, 2.2 Hz, CHOHCH$_2$), 2.62 (1H, dq, J = 9.9, 7.1 Hz, CHCH$_3$) 1.67 (1H, dqd, J = 15.1, 7.5, 2.4 Hz, CH_AH$_B$CH$_3$) 1.45-1.28 (1H, m, CH$_A$$H_BCH_3$), 1.23 (3H, s, C$H_3$CO), 1.18 (3H, d, J = 7.1 Hz, CHCH_3), 0.97

(3H, t, J = 7.3 Hz, CH$_2$CH_3); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ$_C$ 178.0, 89.1, 75.6, 75.2, 41.6, 24.1, 16.4, 12.8, 11.3; IR cm^{-1} ν = 3356 (br. OH), 1748 (C=O); HRMS: *m/z* (ES) 189.1120, C$_9$H$_{17}$O$_4$ [M+H]$^+$ requires 189.1127; $[\alpha]_D^{23}$ = -5.4 (*c* = 1.30 g/100 mL in CHCl$_3$).

(3*S*,4*S*,5*S*)-5-((*S*)-2-(Benzyloxy)-1-hydroxyethyl)-4-hydroxy-3,5-dimethyldihydrofuran-2(3H)-one, 6i: OsO$_4$ (4 mg, 0.02 mmol) was added to a solution of **1i** (75 mg, 0.17 mmol) in acetone/water (8:1, 0.7 mL) followed by addition of NMO (60% by weight in water, 0.03 mL, 0.18 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded **6i** (43 mg, 0.15 mmol, 93%, >49:1 dr). ^{1}H NMR (300 MHz, CDCl$_3$): δ$_H$ 7.31-7.17 (5H, m, Ph), 4.49 (1H, d, J = 11.6 Hz, OCH_AH$_B$Ph), 4.43 (1H, d, J = 11.6 Hz, OCH$_A$$H_B$Ph), 3.86 (1H, d, J = 10.5 Hz, CHCH$_3$CHOH), 3.77 (1H, dd, J = 7.6, 6.2 Hz, CHOHCH$_2$OBn), 3.54 (1H, dd, J = 10.0, 6.2 Hz, CH_AH$_B$OBn), 3.47 (1H, dd, J = 9.8, 7.8 Hz, CH$_A$$H_B$OBn), 3.42 (1H, br. s, O$H$), 2.90 (1H, br. s, O$H$), 2.65-2.53 (1H, m, C$HCH_3$), 1.20-1.16 (6H, m, CHC$H_3$, CC$H_3$); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ$_C$ 175.9, 136.6, 128.9, 128.6, 128.3, 87.7, 76.8, 74.3, 74.0, 70.0, 40.6, 13.9, 12.7; IR cm^{-1} ν = 3420 (OH), 1761 (C=O); HRMS: *m/z* (ES) 281.1368, C$_{15}$H$_{21}$O$_5$, [M+H]$^+$ requires 281.1388; $[\alpha]_D^{23}$ = -12.0 (*c* = 0.50 g/100 mL in CHCl$_3$).

(3*S*,4*S*,5*R*)-4-Hydroxy-5-(2-hydroxypropan-2-yl)-3-methyldihydrofuran-2(3H)-one, 6j: OsO$_4$ (14 mg, 0.05 mmol) was added to a solution of **1j** (184 mg, 0.53 mmol) in acetone/water (8:1, 3 mL) followed by addition of NMO (60% by weight in water, 0.10 mL, 0.59 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded **6j** (38 mg, 0.22 mmol, 41%, 5:1 dr) as a pale oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ$_H$ 4.94 (1H, d, J = 4.1 Hz, OH), 4.26 (1H, app. dt, J = 3.9, 1.5 Hz, CHOH), 4.09 (1H, d, J = 4.1 Hz, CHOCO), 2.96 (1H, br. s, OH), 2.68 (1H, qd, J = 7.8, 1.5 Hz, CHC(CH$_3$)$_2$OH), 1.38 (3H, s, (CH_3)C(CH$_3$)), 1.36 (3H, s, (CH$_3$)C(CH_3)), 1.19

(3H, d, J = 7.8 Hz, CH_3CH); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 179.5, 84.0, 76.3, 73.0, 46.9, 28.7, 25.0, 13.5; IR cm^{-1} ν = 3295 (br. OH), 1754 (C=O); HRMS: m/z (ES) 175.0970, C$_8$H$_{15}$O$_4$ [M+H]$^+$ requires 175.0970; $[\alpha]_D^{23}$ = -55.6 (c = 0.99 g/100 mL in CHCl$_3$).

(3S,4S,5R)-4-Hydroxy-5-(hydroxymethyl)-5-methyl-3-phenyldihydrofuran-2(3H)-one, 6k: OsO$_4$ (6 mg, 0.03 mmol) was added to a solution of **1k** (94 mg, 0.25 mmol) in acetone/water (8:1, 3 mL) followed by addition of NMO (60% by weight in water, 0.06 mL, 0.26 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded **6k** (42 mg, 0.19 mmol, 75%, 9:1 dr) as a pale oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ_H 7.29-7.23 (3H, m, Ph), 7.18-7.13 (2H, m, Ph), 4.62 (1H, d, J = 10.5 Hz, CHOH), 3.80 (1H, d, J = 10.5 Hz, CHCO), 3.70 (1H, d, J = 12.6 Hz, CH_AH$_B$OH), 3.58 (1H, d, J = 12.6 Hz, CH$_A$$H_B$OH), 1.32 (3H, s, C$H_3$); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 174.3, 135.1, 129.4, 129.0, 128.4, 86.5, 75.3, 65.5, 53.8, 16.9; IR IR cm^{-1} ν = 3308 (br. OH), 1745 (C=O); HRMS: m/z (ES) 223.0961, C$_{12}$H$_{15}$O$_4$ [M+H]$^+$ requires 223.0970; $[\alpha]_D^{23}$ = -9.1 (c = 0.83 g/100 mL in MeOH).

(3S,4S,5S)-5-((R)-2-(benzyloxy)-1-hydroxyethyl)-4-hydroxy-3-methyldihydrofuran-2(3H)-one, 6g: AD-mix-β (252 mg, 1.4 g/mmol of allylic alcohol) was dissolved in a 1:1 mixture of ^{t}BuOH and water (1.8 mL, 10 mL/mmol of allylic alcohol). MeSO$_2$NH$_2$ (17 mg, 0.18 mmol) was added and the biphasic suspension was cooled to 0 ˚C. (S)-4-Benzyl-3-((2S,3R,Z)-6-(benzyloxy)-3-hydroxy-2-methylhex-4-enoyl)-5,5-dimethyloxazolidin-2-one (80 mg, 0.18 mmol) dissolved in CH$_2$Cl$_2$ (1 mL) was added dropwise *via* syringe to the stirring suspension followed by OsO$_4$ (4.5 mg, 0.18 mmol). The suspension was stirred vigorously whilst slowly warming to room temperature. After 48 hours, the reaction was quenched with solid sodium sulfite (100 mg) at room temperature. The suspension was filtered through a pad of Celite®/Florisil®, eluting with ethyl acetate before the solution was

dried over MgSO$_4$ and concentrated. The crude product was purified *via* column chromatography [1:1 EtOAc:Petroleum ether, R$_f$ 0.15] to afford (3*S*,4*S*,5*S*)-5-((*R*)-2-(benzyloxy)-1-hydroxyethyl)-4-hydroxy-3-methyldihydrofuran-2(3H)-one **6g** (46 mg, 0.17 mmol, 95%, 17:1 dr) as a white oil.

(3*S*,4*S*,5*R*)-5-((*S*)-2-(Benzyloxy)-1-hydroxyethyl)-4-hydroxy-3-methyldihydrofuran-2(3H)-one, 8: AD-mix-α (252 mg, 1.4 g/mmol of allylic alcohol) was dissolved in a 1:1 mixture of ^{t}BuOH and water (1.8 mL, 10 mL/mmol of allylic alcohol). MeSO$_2$NH$_2$ (17 mg, 0.18 mmol) was added and the biphasic suspension was cooled to 0 °C. (*S*)-4-Benzyl-3-((2*S*,3*R*,Z)-6-(benzyloxy)-3-hydroxy-2-methylhex-4-enoyl)-5,5-dimethyloxazolidin-2-one (80 mg, 0.18 mmol) dissolved in CH$_2$Cl$_2$ (1 mL) was added dropwise *via* syringe to the stirring suspension followed by OsO$_4$ (4.5 mg, 0.18 mmol). The suspension was stirred vigorously whilst slowly warming to room temperature. After 48 hours, the reaction was quenched with solid sodium sulfite (100 mg) at room temperature. The suspension was filtered through a pad of Celite®/Florisil®, eluting with ethyl acetate before the solution was dried over MgSO$_4$ and concentrated. The crude product was purified using *via* column chromatography [1:1 EtOAc:Petroleum ether, R$_f$ 0.15] to afford (3*S*,4*S*,5*R*)-5-((*S*)-2-(benzyloxy)-1-hydroxyethyl)-4-hydroxy-3-methyldihydrofuran-2(3H)-one **8** (46 mg, 0.17 mmol, 95%, 4:1 dr) as a white oil.

Synthesis of 2-Deoxy-D-ribonolactone

(*S*)-4-Benzyl-3-(2-chloroacetyl)-5,5-dimethyloxazolidin-2-one, 7c: The title compound was prepared according to the general procedure from *n*-BuLi (10.7 mL, 26.8 mmol, 2.5 M solution in hexane), (*S*)-4-benzyl-5,5-dimethyloxazolidin-2-one (5.00 g, 24.3 mmol) and chloroacetyl chloride (2.07 mL, 26.8 mmol) in THF (150 mL). The crude product was purified using flash silica chromatography [1:9 EtOAc:Petroleum ether, R$_f$ 0.50] to afford

(*S*)-4-benzyl-3-(2-chloroacetyl)-5,5-dimethyloxazolidin-2-one **7c** (5.69 g, 20.1 mmol, 83%) as a colourless oil that solidified on standing. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.32-7.20 (5H, m, Ph), 4.76 (1H, d, *J* = 15.8 Hz, COC*H*$_A$H$_B$Cl), 4.64 (d, *J* = 15.8 Hz, COCH$_A$*H*$_B$Cl), 4.49 (1H, dd, *J* = 9.7, 3.9 Hz, C*H*N), 3.20 (1H, dd, *J* = 14.4, 3.8 Hz, CH*H*$_A$H$_B$Ph), 2.88 (1H, dd, *J* = 14.4, 9.8 Hz, CH$_A$*H*$_B$Ph), 1.38 (3H, s, C(C*H*$_3$)(CH$_3$)), 1.36 (3H, s, C(CH$_3$)(C*H*$_3$)); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 166.4, 152.4, 136.5, 129.1, 128.9, 127.1, 83.7, 64.1, 44.0, 35.0, 28.7, 22.4; IR cm^{-1} ν = 1769 (C=O$_{ox}$), 1709 (C=O); HRMS: *m/z* (ES) 304.0722, C$_{14}$H$_{16}$ClNNaO$_3$ [M+Na]$^+$ requires 304.0716; $[\alpha]_D^{25}$ = -32.0 (*c* = 0.50 g/100 mL in CHCl$_3$).

(*S*)-4-Benzyl-3-((2*S*,3*R*)-2-chloro-3-hydroxypent-4-enoyl)-5,5-dimethyloxazolidin -2-one, 9: The title compound was prepared according to the general procedure from dibutylboron triflate (7.70 mL, 7.7 mmol), (*S*)-4-benzyl-3-(2-chloroacetyl)-5,5-dimethyloxazolidin-2-one **7c** (1.97g, 7.0 mmol), *N*,*N*-diisopropylethylamine (1.58 mL, 9.1 mmol) and acrolein (0.61 mL, 9.1 mmol) in dichloromethane (15 mL) to afford a crude product as a pale yellow oil. The crude product was purified using flash silica chromatography [1:4 EtOAc:Petroleum ether, R$_f$ 0.27] to afford (*S*)-4-benzyl-3-((2*S*,3*R*)-2-chloro-3-hydroxypent-4-enoyl)-5,5-dimethyloxazolidin-2-one **9** (1.07g, 3.2 mmol, 45%) as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.31-7.17 (5H, m, Ph), 5.88 (1H, ddd, *J* = 17.3, 10.5, 5.8 Hz, C*H*=CH$_2$), 5.72 (1H, d, *J* = 5.1 Hz, C*H*Cl), 5.40 (1H, dt, *J* = 17.3, 1.3 Hz, CH=C*H*$_A$H$_B$), 5.28 (1H, dt, *J* = 10.5, 1.2 Hz, CH=CH$_A$*H*$_B$), 4.59 (1H, app. t, *J* = 5.5 Hz, C*H*OH), 4.48 (1H, dd, *J* = 9.5, 3.8 Hz, C*H*N), 3.14 (1H, dd, *J* = 14.4, 3.8 Hz C*H*$_A$H$_B$Ph), 3.00 (1H, br. s, O*H*), 2.88 (1H, dd, *J* = 14.4, 9.5 Hz, CH$_A$*H*$_B$Ph), 1.36 (3H, s, C(C*H*$_3$)(CH$_3$)), 1.33 (3H, s, C(CH$_3$)(C*H*$_3$)); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 167.9, 152.0, 136.4, 135.0, 129.1, 128.8, 127.0, 118.9, 83.3, 72.9, 64.0, 59.1, 34.9, 28.5, 22.2; IR cm^{-1} ν = 3496 (OH), 1771 (C=O$_{ox}$), 1703 (C=O); HRMS: *m/z* (ES) 338.1149, C$_{17}$H$_{21}$ClNO$_4$ [M+H]$^+$ requires 338.1159; $[\alpha]_D^{24}$ = -12.0 (*c* = 1.00 g/100 mL in CHCl$_3$).

(S)-4-Benzyl-3-((S)-3-hydroxypent-4-enoyl)-5,5-dimethyloxazolidin-2-one, 10: (S)-4-Benzyl-3-((2S,3R)-2-chloro-3-hydroxypent-4-enoyl)-5,5-dimethyloxazolidin-2-one **9** (1.08 g, 3.2 mmol) was dissolved in dry methanol (12 mL) under nitrogen. Zinc dust (0.83 g, 12.8 mmol) and ammonium chloride (0.69 g, 12.8 mmol) were added and the reaction was stirred for one hour. The suspension was filtered through Celite and concentrated to afford the crude product as a yellow oil. The crude product was purified using flash silica chromatography [1:4 EtOAc:Petroleum ether, R_f 0.18] to afford (S)-4-benzyl-3-((S)-3-hydroxypent-4-enoyl)-5,5-dimethyloxazolidin-2-one **10** (0.79 g, 2.6 mmol, 82%) as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H 7.33-7.24 (5H, m, Ph), 5.89 (1H, ddd, J = 17.3, 10.5, 5.4 Hz, CH=CH$_2$), 5.32 (1H, d, J = 17.3 Hz, CH=CH_AH$_B$), 5.15 (1H, d, J = 10.5 Hz, CH=CH$_A$$H_B$), 4.58-4.50 (2H, m, C$HOH, CH$N), 3.16-3.09 (3H, m, C$H_ACH_BPh, CH_2$CHOH), 2.93-2.85 (2H, m, CH$_A$CH_BPh, CHOH), 1.39 (3H, s, C(CH_3)(CH$_3$)), 1.37 (3H, s, C(CH$_3$)(CH_3)); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$): δ_C 172.3, 152.7, 138.8, 136.8, 129.1, 128.9, 127.0, 115.5, 82.7, 68.9, 63.5, 42.6, 35.6, 28.6, 22.3; IR cm^{-1} ν = 3483 (OH), 1771 (C=O), 1694 (C=O$_{ox}$); HRMS: m/z (ES) 304.1511, C$_{17}$H$_{22}$NO$_4$, [M+H]$^+$ requires 304.1548; $[\alpha]_D^{20}$ = -52.0 (c = 0.50 g/100 mL in CHCl$_3$).

2-Deoxy-D-ribonolactone - (4S,5R)-4-Hydroxy-5-(hydroxymethyl)dihydrofuran-2(3H)-one, 11: OsO$_4$ (16 mg, 0.06 mmol) was added to a solution of **10** (200 mg, 0.66 mmol) in acetone/water (8:1, 2.5 mL) followed by addition of NMO (60% by weight in water, 0.12 mL, 0.73 mmol) according to the general procedure to afford the crude product as black oil. Purification *via* column chromatography afforded **11** (76 mg, 0.57 mmol, 87%, 9:1 dr).
(4S,5R)-major: ^{1}H NMR (500 MHz, MeOD): δ_H 4.46 (1H, dt, J = 6.7, 2.3 Hz, CHOH), 4.40–4.39 (1H, m, CHCH$_2$OH), 3.79 (1H, dd, J = 12.4, 3.3 Hz, CH_AH$_B$OH), 3.72 (1H, dd, J = 12.4, 3.7 Hz, CH$_A$$H_B$OH), 2.94 (1H, dt, J = 17.9, 6.8 Hz, CH_AH$_B$C=O), 2.40 (1H, dd, J = 17.9, 2.5 Hz, CH$_A$$H_B$C=O); ^{13}C{^{1}H} NMR (75 MHz, MeOD): δ_C 179.5, 91.0, 70.6, 63.4,

40.0; **(4*S*,5*S*)-minor:** ^{1}H NMR (500 MHz, MeOD): δ_H 4.63-4.50 (2H, m, C*H*OH & C*H*CH$_2$OH), 3.90 (2H, dd, *J* = 5.4, 1.6 Hz, C*H*$_2$OH), 2.93 (1H, dd, *J* = 17.6, 5.9 Hz, C*H*$_A$H$_B$C=O), 2.45 (1H, dd, *J* = 17.7, 1.6 Hz, CH$_A$C*H*$_B$C=O); ^{13}C{^{1}H} NMR (75 MHz, MeOD): δ_C 179.5, 87.4, 69.8, 62.1, 40.9; IR cm^{-1} ν = 3356 (OH), 1749 (C=O); HRMS: *m/z* (ES) 155.0333, C$_5$H$_8$NaO$_4$, [M+Na]$^+$ requires 155.0320; $[\alpha]_D^{25}$ = +4.0 (*c* = 0.50 g/100 mL in MeOH) [lit: $[\alpha]_D^{25}$ = +2.17 (*c* = 0.6 g/100 mL in MeOH)].[12a]

Acknowledgements

Supporting Information

^{1}H, ^{13}C{^{1}H}, spectra of all aldol products (**1a-k**, **9**) and hydroxy-γ-butyrolactones (**6a-k**, **8**, **11**) as well as ^{1}H NOE spectra of all lactones. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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