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N-Acyl-5,5-dimethyloxazolidin-2-ones as latent aldehyde equivalents

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A study of the properties of *N*-hydrocinnamoyl- derivatives of 5,5-dimethyloxazolidin-2-one, 4,4-dimethyloxazolidin-2-one and oxazolidin-2-one upon hydride reduction with DIBAL-H demonstrates that the 5,5-dimethyl-group is essential for inhibition of endocyclic nucleophilic attack. For instance, treatment of *N*-hydrocinnamoyl-5,5-dimethyloxazolidin-2-one with DIBAL-H results in the selective formation of the stable *N*-1′-hydroxyalkyl derivative which may be regarded as a masked hydrocinnamaldehyde equivalent, as treatment under basic conditions affords the parent aldehyde in excellent yield. Treatment of *N*-hydrocinnamoyl-4,4-dimethyloxazolidin-2-one with DIBAL-H under identical conditions affords a complex mixture of products, including the formate ester product of endocyclic cleavage. As an alternate strategy, DIBAL-H reduction of straight chain and branched *N*-acyl-5,5-dimethyloxazolidin-2-one derivatives, followed by a Horner–Wadsworth–Emmons reaction affords α,β-unsaturated esters in good yields. Branching α- to the exocyclic carbonyl in *N*-acyl-oxazolidinones inhibits DIBAL-H reduction, but this can be overcome by precomplexation with $ZnCl_2$, with subsequent fragmentation generating either the corresponding aldehyde or α,β-unsaturated esters. The addition of $ZnCl_2$ has been shown to increase the diastereoselectivity observed in Wadsworth–Horner–Emmons reactions of lithiated phosphonates.

Introduction

The use of *N*-acyl derivatives of chiral auxiliaries to prepare homochiral molecular fragments is well established within organic synthesis.[1] Most recyclable auxiliaries readily allow the release of attached molecular fragments at either the carboxylic acid or the alcohol oxidation level upon hydrolysis or exhaustive reduction respectively. However direct transformation to the corresponding aldehyde is an equally desirable synthetic transformation, as demonstrated by the reductions of *N*-acylsultam[2] and pseudoephedrine[3] fragments to the corresponding aldehydes. The conversion of *N*-acyloxazolidin-2-ones to the corresponding aldehydes can typically be achieved using only two step protocols, involving reduction to the alcohol followed by re-oxidation to aldehyde[4] or conversion of the carboxylic acid fragment to its Weinreb amide followed by reduction with DIBAL-H.[5] The reductive cleavage properties of Weinreb amides are thought to arise from the stability of the tetrahedral, possibly chelated, intermediates such as **1**, which fragment upon hydrolytic work-up to release the aldehyde.[6] As part of our ongoing studies concerning the utility of oxazolidinones in synthesis, it was reasoned that *N*-acyloxazolidin-2-ones could be engineered to exhibit identical cleavage properties to those of Weinreb amides, while, in contrast,[7] simultaneously being amenable to enolate based reactions. It was proposed that a lone-pair of the endocyclic oxazolidin-2-one carbonyl of **2** would have the capacity to stabilise the tetrahedral intermediate **3** arising from reduction of the exocyclic carbonyl of **2** with DIBAL-H, with the resulting chelated aluminium complex being inert to further reduction. This would enable *N*-acyloxazolidin-2-ones to function as latent aldehyde equivalents, avoiding over-reduction to the corresponding alcohol (Fig. 1).

At the onset of this programme of research, limited literature precedent existed for the direct reduction of *N*-acyloxazolidin-2-ones to aldehydes,[8] although Meyers *et al.* had reported an isolated example of the reduction of an *N*-acyloxazolidin-2-one with Red-Al in THF at −78 °C to the corresponding aldehyde.[9] The structurally related *N*-acyloxazolidin-2-thiones allow the direct synthesis of aldehydes upon reductive treatment with

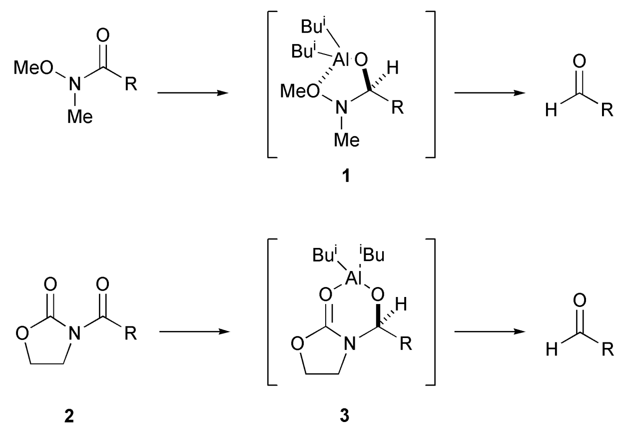

Fig. 1

either DIBAL-H or lithium tri-*tert*-butoxyaluminium hydride,[10] although the wide applicability of this class of auxiliary within synthesis is yet to be realised.[11] In the light of these reports, a full investigation concerning the reductive behaviour of a range of achiral oxazolidin-2-ones upon treatment with DIBAL-H was initiated. Part of this work concerning the stability of the tetrahedral intermediate arising from DIBAL-H reduction of *N*-acyl-5,5-dimethyloxazolidin-2-ones (similar tetrahedral carbinols have been reported subsequently by Evans *et al.* upon reduction of *N*-acylpyrroles)[12] has been the subject of a preliminary communication.[13]

Results and discussion

Evaluation of *N*-hydrocinnamoyl derivatives of 5,5-dimethyloxazolidin-2-one, 4,4-dimethyloxazolidin-2-one and oxazolidin-2-one as latent aldehyde equivalents

Previous studies from within this laboratory concerning the use of oxazolidin-2-ones for asymmetric transformations have shown that the presence of the *gem*-dimethyl groups at C(5) of

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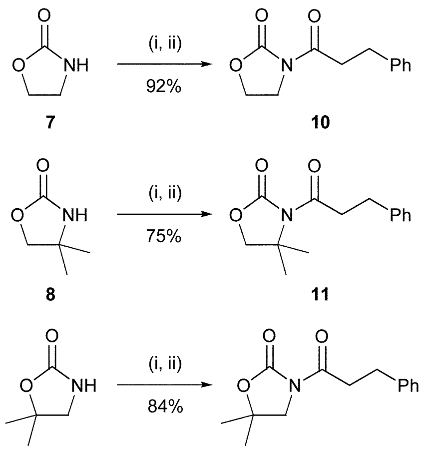
oxazolidinone auxiliaries is crucial to inhibit endocyclic attack in hydrolytic cleavage reactions of *N*-acyloxazolidin-2-ones.[14] The presence and position of the *gem*-dimethyl groups were expected to affect the reductive cleavage properties of *N*-acyl-oxazolidin-2-ones upon treatment with DIBAL-H in the same manner. In order to investigate this structural requirement, parent oxazolidin-2-one **7**,[15] 4,4-dimethyloxazolidinone **8**,[16] and 5,5-dimethyloxazolidinone **9**[17] were prepared following literature procedures and subsequently deprotonated with *n*-BuLi at −78 °C before being *N*-acylated with hydrocinnamoyl chloride[18] to furnish *N*-hydrocinnamoyloxazolidin-2-ones **10**–**12** respectively in high yield (Scheme 1).



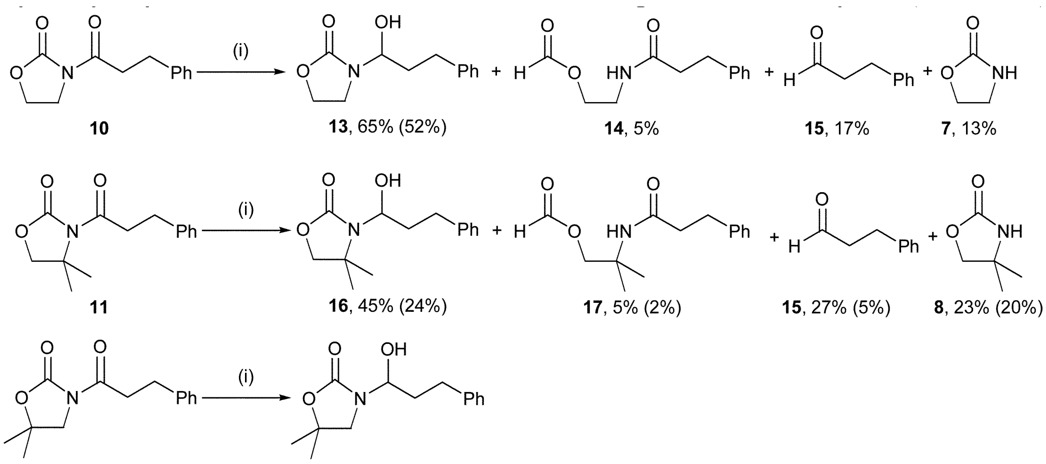
Scheme 1 *Reagents and conditions*: (i). *n*-BuLi, THF, −78 °C; (ii). $PhCH_2CH_2COCl$, THF, −78 °C to rt.

Treatment of *N*-hydrocinnamoyloxazolidin-2-ones **10**–**12** with DIBAL-H allowed the relative propensity of each oxazolidinone auxiliary to discourage endocyclic attack over exocyclic attack to be determined by analysis of the product distribution. Both the parent *N*-hydrocinnamoyl oxazolidinone **10**[19] and *N*-hydrocinnamoyl 4,4-dimethyloxazolidinone **11** {ν_{max} (C=O$_{endocyclic}$) 1777 cm^{-1}, (C=O$_{exocyclic}$) 1703 cm^{-1}, δ_C C(1′) 154.1} afforded complex mixtures of products upon treatment with DIBAL-H, with purification of the crude reaction mixture resulting from reduction of **11** by repeated silica gel chromatography affording the formate ester product of endocyclic cleavage **17**, 1′-hydroxyalkyl-4,4-dimethyloxazolidinone **16** {ν_{max} (C=O$_{endocyclic}$) 1737 cm^{-1}, δ_C C(1′) 77.6}, hydrocinnamaldehyde **15** and 4,4-dimethyloxazolidinone **8**. The product distribution formed from reduction of *N*-hydrocinnamoyl-oxazolidinone **10** was similarly determined by integration of the characteristic peaks in the ^{1}H 400 MHz NMR spectrum of the crude reaction mixture, with 1′-hydroxyalkyloxazolidinone **13** {ν_{max} (C=O$_{endocyclic}$) 1730 cm^{-1}, δ_C C(1′) 77.0} being isolated in 52% yield after chromatography. While the proportions of endocyclic cleavage product **14** and **17** arising from reduction of the unsubstituted and 4,4-dimethyl substituted *N*-acyl-oxazolidinones **10** and **11** are identical, the proportion of aldehyde **15** is greater from reduction of **11**, suggesting that the presence of substituents at C(4) of the oxazolidin-2-one fragment destabilizes the intermediate tetrahedral complex, facilitating fragmentation to aldehyde **15**. In contrast, DIBAL-H reduction of *N*-hydrocinnamoyl 5,5-dimethyloxazolidinone **12** {ν_{max} (C=O$_{endocyclic}$) 1757 cm^{-1}, (C=O$_{exocyclic}$) 1697 cm^{-1}, δ_C C(1′) 152.8} yielded the 1′-hydroxyalkyloxazolidinone **18** {ν_{max} (C=O$_{endocyclic}$) 1730 cm^{-1}, δ_C C(1′) 76.7} as the exclusive product, which was isolated in 74% yield after purification by chromatography. Furthermore, reduction of *N*-hydrocinnamoyl 5,5-dimethyloxazolidinone **12** with $LiAlH_4$ (1 equivalent relative to hydride) also returned 1′-hydroxy-alkyloxazolidinone **18** as the sole reaction product in 80% yield (Scheme 2).

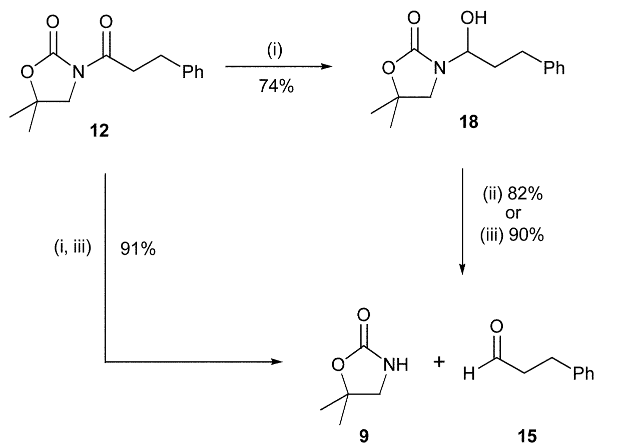
Having demonstrated the 5,5-dimethyloxazolidinone auxiliary successfully suppresses endocyclic C=O reduction in its *N*-hydrocinnamoyl derivative **12**, the controlled fragmentation of 1′-hydroxyalkyloxazolidin-2-one **18** to the corresponding aldehyde was investigated. Initial attempts concentrated upon the use of basic reaction conditions, with NaH in THF returning a complex mixture of products, although the use of K_2CO_3 in MeOH efficiently promoted the desired fragmentation, giving hydrocinnamaldehyde **15** in 82% yield. An alternative synthetic protocol for the production of aldehyde **15** from oxazolidinone **18** allowed for its *in situ* trapping, *via* formation of an intermediate bisulfite adduct. Treatment of **18** with sodium hydrogen sulfate (adjusted to pH 9.0 with sodium hydroxide) and subsequent treatment with 1 M HCl$_{(aq)}$ and chromatography gave aldehyde **15** in 90% yield. This procedure was further modified to allow a 'one-pot' process involving consecutive treatment of **12** with DIBAL-H in DCM at −78 °C, followed immediately by the bisulfite trapping protocol, to afford aldehyde **15** in 91% yield upon acidic work-up (Scheme 3).

A DIBAL-H Wadsworth–Horner–Emmons homologation protocol

Since aldehydes such as **15** are highly reactive species, readily undergoing a variety of reactions including aldol and trimerisation reactions, they are typically generated as reactive synthetic intermediates, immediately being prepared and

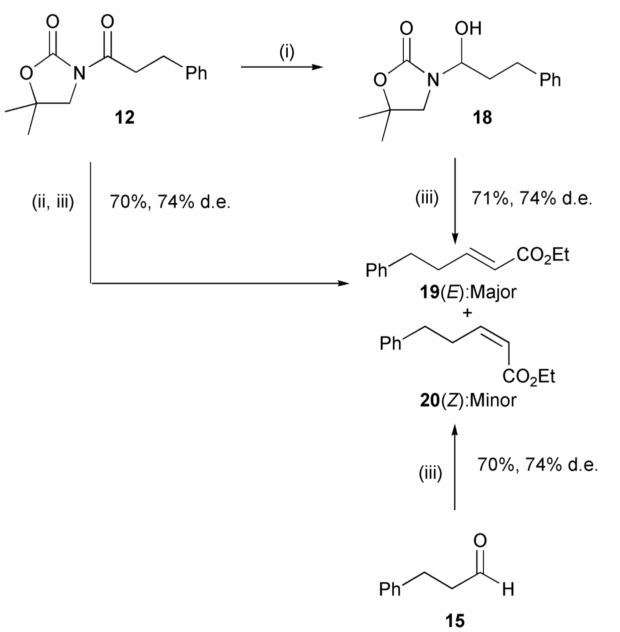


Scheme 2 *Reagents and conditions*: (i) DIBAL-H, DCM, −78 °C; ratio of products determined by integration of resonances in the ^{1}H NMR 400 MHz spectra of the crude product mixtures; isolated yields of components given in brackets.



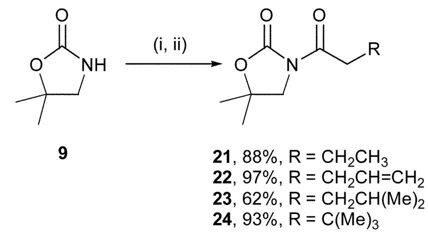
Scheme 3 *Reagents and conditions*: (i) DIBAL-H, DCM, −78 °C; (ii) K_2CO_3, MeOH, rt; (iii) NaOH, $NaHSO_3$ then 1 M $HCl_{(aq)}$.

transformed, for instance by the use of Wittig or Wadsworth–Horner–Emmons methodologies. In this case, the development of a DIBAL-H/Wadsworth–Horner–Emmons strategy for the transformation of *N*-hydrocinnamoyloxazolidin-2-one **12** to its corresponding α,β-unsaturated ester was investigated, as it was reasoned that deploying the lithium anion of a phosphonate to promote the fragmentation of 1′-hydroxyalkyloxazolidin-2-one **18** would afford aldehyde **15** *in situ*, which would be immediately trapped by excess phosphonate anion to afford the desired α,β-unsaturated ester. To test this theory, 1′-hydroxyalkyloxazolidin-2-one **18** was treated with 2.5 equivalents of the lithium anion of triethyl phosphonoacetate, giving a mixture of the chromatographically separable (*E*) and (*Z*)-α,β-unsaturated esters **19** and **20** in 71% overall yield and 74% de, plus the parent oxazolidin-2-one **9** in 70% yield. Both the yield and diastereoselectivity obtained from this protocol were identical to those obtained for reaction of the parent aldehyde **15** with the lithium anion of triethyl phosphonoacetate. Extension of this DIBAL-H/Wadsworth–Horner–Emmons methodology to the development of a 'one-pot' protocol involving sequential treatment of *N*-hydrocinnamoyloxazolidin-2-one **12** with DIBAL-H and the lithium anion of triethyl phosphonoacetate similarly gave **19**–**20** in 70% yield and in 74% de (Scheme 4).



Scheme 4 *Reagents and conditions*: (i) DIBAL-H, DCM, −78 °C; (ii) DIBAL-H, THF, −78 °C; (iii) $(EtO)_2POCH(Li)CO_2Et$, THF, −78 °C to rt.

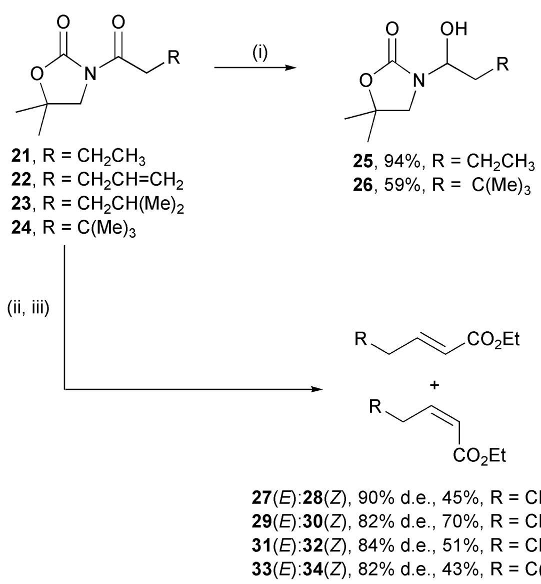
Having demonstrated that *N*-hydrocinnamoyl-5,5-dimethyloxazolidin-2-one **12** can be regarded as a latent aldehyde equivalent *via* fragmentation of its *N*-1′-hydroxyalkyl derivative and trapping with a phosphonate anion, the generality of this protocol was investigated. A series of *N*-acyl-5,5-dimethyloxazolidinones were therefore prepared by deprotonation of 5,5-dimethyloxazolidinone **9** with *n*-BuLi and subsequent *N*-acylation with a range of straight chain and branched acid chlorides, furnishing *N*-acyl-5,5-dimethyloxazolidin-2-ones **21**–**24** in good yields (Scheme 5).



Scheme 5 *Reagents and conditions*: (i) *n*-BuLi, THF, −78 °C; (ii) RCH_2COCl, THF, −78 °C to rt.

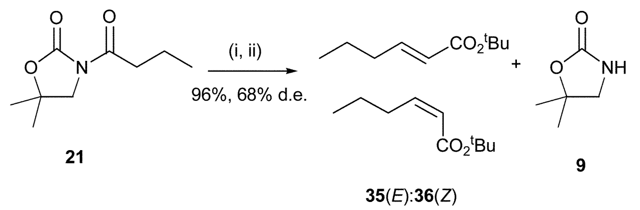
Treatment of *N*-acyl-5,5-dimethyloxazolidin-2-ones **21**–**24** with DIBAL-H at −78 °C in DCM furnished the corresponding 1′-hydroxyalkyloxazolidinones as the sole reaction products upon standard work up. However, although 1′-hydroxyalkyloxazolidinone **18** exhibits a high degree of stability towards mildly acidic conditions thereby allowing purification by flash column chromatography, attempted purification of 1′-hydroxyalkyloxazolidinones **25** and **26** on silica promoted partial decomposition and furnished a mixture of unidentified products. Therefore **25** {ν_{max} (C=O$_{endocyclic}$) 1741 cm^{-1}, δ_C C(1′) 76.7} and **26** {ν_{max} (C=O$_{endocyclic}$) 1732 cm^{-1}, δ_C C(1′) 75.3} were characterised directly from the crude reaction mixture. As a result of the propensity of 1′-hydroxyalkyloxazolidinones **25** and **26** to fragmentation upon purification, application of the tandem DIBAL-H/Wadsworth–Horner–Emmons reaction protocol was considered. Thus, successive treatment of **21**–**24** with DIBAL-H and the lithium anion of triethyl phosphonoacetate gave the requisite α,β-unsaturated esters **27**–**34** in 43–70% overall yield, and in 82–90% de (Scheme 6).

Analysis of the ^{1}H NMR spectra of the crude reaction mixtures arising from these reactions, in conjunction with observed losses in mass balance during purification were ascribed to the



Scheme 6 *Reagents and conditions*: (i) DIBAL-H, DCM, −78 °C; (ii) DIBAL-H, THF, −78 °C; (iii) $(EtO)_2POCH(Li)CO_2Et$, THF, −78 °C to rt.

volatility of the target α,β-unsaturated ethyl esters. As a result, the tandem DIBAL-H–Wittig protocol was repeated on *N*-butyroyl-5,5-dimethyloxazolidin-2-one **21** using the lithium anion of *tert*-butyl dimethylphosphonoacetate, furnishing the α,β-unsaturated-*tert*-butyl esters **35**–**36** in 96% isolated yield and in 68% de (Scheme 7).

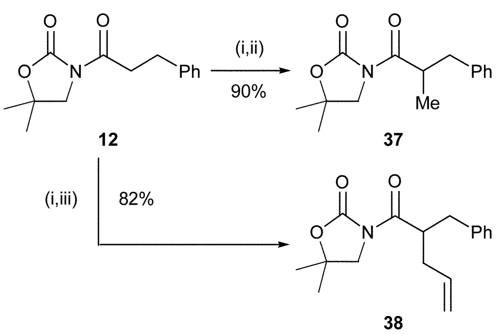


Scheme 7 *Reagents and conditions:* (i) DIBAL-H, THF, −78 °C; (ii) $(MeO)_2POCH(Li)CO_2{}^tBu$, THF, −78 °C to rt.

The tandem protocol using *tert*-butyl dimethylphosphonoacetate therefore represents the most efficient *in situ* Wadsworth–Horner–Emmons trap for fragmentation of *N*-butyryl-5,5-dimethyloxazolidinone **21** (96% yield), with much improved efficiency with respect to the use of triethyl phosphonoacetate (45% yield).

Synthesis of α-substituted aldehydes

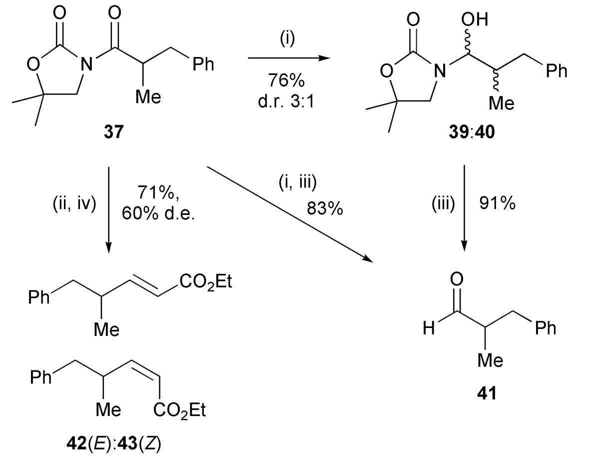
Having shown that straight chain and branched *N*-acyl-5,5-dimethyloxazolidin-2-ones may be regarded as latent aldehyde equivalents, attention turned to the reductive cleavage of their α-substituted analogues. As Weinreb amides are incompatible with enolate formation and hence cannot be taken through many general synthetic protocols,[7] the development of latent aldehyde equivalents compatible with such methodology would prove synthetically useful.[20] *N*-Hydrocinnamoyl-5,5-dimethyloxazolidin-2-one **12** was therefore treated with LHMDS at 0 °C followed by alkylation with either methyl iodide or allyl bromide to afford the α-alkylated oxazolidinones **37** and **38** respectively (Scheme 8).



Scheme 8 *Reagents and conditions:* (i) LHMDS, THF, 0 °C; (ii) MeI, THF, 0 °C; (iii) $CH_2{=}CHCH_2Br$, THF, 0 °C.

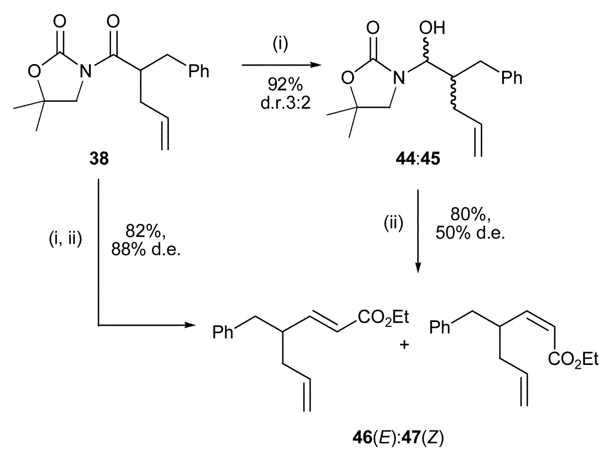
Treatment of α-methyloxazolidinone **37** with DIBAL-H in THF at −78 °C gave a chromatographically stable 3 : 1 diastereomeric mixture of 1′-hydroxyalkyloxazolidinones **39** : **40** {ν_{max} ($C{=}O_{endocyclic}$) 1754 cm^{-1}; δ_C C(1′) major diastereoisomer 81.0, δ_C C(1′) minor diastereoisomer 81.3}. Treatment of this diastereoisomeric mixture with NaOH–$NaHSO_3$ afforded, after acidic work up, 2-methylhydrocinnamaldehyde **41** in 91% isolated yield. The corresponding 'one pot' procedure afforded the desired aldehyde **41** in 83% yield directly from *N*-α-methylhydrocinnamoyl-5,5-dimethyloxazolidin-2-one **37**. Application of the tandem DIBAL-H/Wadsworth–Horner–Emmons methodology similarly proved efficient, affording the γ-methyl-α,β-unsaturated ester **42** : **43** in 71% overall yield and in 60% de (Scheme 9).

However, treatment of the α-allylated *N*-acyloxazolidin-2-one **38** with DIBAL-H under the standard reduction conditions



Scheme 9 *Reagents and conditions*: (i) DIBAL-H, DCM, −78 °C; (ii) DIBAL-H, THF, −78 °C; (iii) NaOH, $NaHSO_3$ then 1 M $HCl_{(aq)}$; (iv) $(EtO)_2POCH(Li)CO_2Et$, THF, −78 °C to rt.

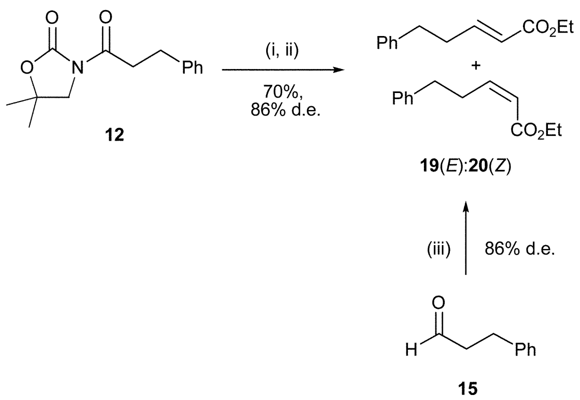
returned only starting material with no evidence of any reduction, even after treatment with excess DIBAL-H (3 eq.) at rt for 15 hours. It was proposed that the low propensity of *N*-acyloxazolidin-2-one **38** towards reduction with DIBAL-H may be overcome by increasing its reactivity *via* precoordination with a Lewis acid. $ZnCl_2$ was chosen as the activating agent for this transformation, since Arai *et al.* have used the DIBAL-H–$ZnCl_2$ combination to great effect for the diastereoselective reductions of the carbonyl group in β-ketosulfoxides.[21] Based on this literature protocol, α-allylated *N*-acyloxazolidin-2-one **38** was treated successively with $ZnCl_2$ and then DIBAL-H in THF at −30 °C, giving an inseparable 3 : 2 mixture of the chromatographically stable diastereoisomeric 1′-hydroxyalkyloxazolidinones **44**–**45** {ν_{max} ($C{=}O_{endocyclic}$) 1717 cm^{-1}; δ_C C(1′) major diastereoisomer 79.1, δ_C C(1′) minor diastereoisomer 79.5} in 92% isolated yield. Treatment of this diastereoisomeric mixture with the lithium anion of triethyl phosphonoacetate gave the γ-allyl-α,β-unsaturated esters **46**–**47** in 80% yield and 50% de, while application of the $ZnCl_2$ activation protocol to a 'one pot' procedure on the allylated derivative **38** furnished **46**–**47** in 82% yield, but with a notable increase in diastereoselectivity, giving **46**–**47** in 88% de (Scheme 10).



Scheme 10 *Reagents and conditions:* (i) $ZnCl_2$; DIBAL-H, THF, −30 °C; (ii) $(EtO)_2POCH(Li)CO_2Et$, THF, −78 °C.

This remarkable increase in diastereoselectivity between the stepwise (50% de) and $ZnCl_2$ initiated tandem (88% de) reaction manifolds for this Wadsworth–Horner–Emmons olefination reaction deserved further investigation. The $ZnCl_2$–DIBAL-H/Wadsworth–Horner–Emmons procedure was therefore performed on *N*-hydrocinnamoyl-5,5-dimethyloxazolidinone **12**, furnishing the α,β-unsaturated esters **19**–**20** in 70% yield and in

86% de, a marked improvement upon the 74% de previously seen without the presence of $ZnCl_2$. Further to this observation, hydrocinnamaldehyde **15** was treated with $ZnCl_2$ followed by the lithium anion of triethyl phosphonoacetate, similarly furnishing α,β-unsaturated esters **19**–**20** in 86% de, identical to that noted in the tandem $ZnCl_2$–DIBAL-H/Wadsworth–Horner–Emmons protocol (Scheme 11).



Scheme 11 *Reagents and conditions*: (i) $ZnCl_2$, DIBAL-H, THF, −30 °C; (ii) $(EtO)_2POCH(Li)CO_2Et$, THF, −78 °C to rt; (iii) $ZnCl_2$, −30 °C then $(EtO)_2POCH(Li)CO_2Et$, THF, −78 °C to rt.

Previous investigations by Masamune *et al.* concerning the reactivity of Wadsworth–Horner–Emmons reactions have shown that the addition of LiCl allows the use of mild bases such as DBU to promote efficient olefination reactions,[22] while Nagao *et al.* have shown that $Sn(OSO_2CF_3)_2$ and *N*-ethylpiperidine[23] has a similar effect. In this case, however, it appears that the addition of $ZnCl_2$ plays an additional role in increasing the diastereoselectivity of the Wadsworth–Horner–Emmons reaction. Although a related effect has been reported by Seebach *et al.*, with the addition of $ZnBr_2$ increasing the diastereoselectivity upon alkylation of chiral *N*-acyloxazolidinones,[24] the scope and limitations of the $ZnCl_2$ modification of the Wadsworth–Horner–Emmons olefination protocol, and the exact role of $ZnCl_2$ in this procedure, are currently under investigation.

Conclusion

N-Acyl-5,5-dimethyloxazolidin-2-ones can be considered as latent aldehyde equivalents. Direct DIBAL-H reduction of *N*-acyl-5,5-dimethyloxazolidin-2-ones produces the corresponding 1′-hydroxyalkyloxazolidinone, which may be fragmented to the parent aldehyde and the oxazolidinone auxiliary by treatment with either K_2CO_3 in MeOH or sodium hydrogen sulfate (adjusted to pH 9.0 with sodium hydroxide) and subsequent acidic work up. Alternatively, treatment of the 1′-hydroxyalkyloxazolidinones with lithiated triethyl phosphonoacetate gives α,β-unsaturated esters. The presence of a substituent α- to the exocyclic carbonyl in *N*-acyloxazolidinones may inhibit DIBAL-H reduction, but this can be overcome by precomplexation with $ZnCl_2$ to give the corresponding 1′-hydroxyalkyloxazolidinone, which may be fragmented to generate either the corresponding aldehyde or α,β-unsaturated esters. The addition of $ZnCl_2$ also serves to increase the diastereoselectivity observed in Wadsworth–Horner–Emmons reactions.

Experimental

General experimental

All reactions involving organometallic or other moisture sensitive reagents were performed under an atmosphere of nitrogen *via* standard vacuum line techniques. All glassware was flame-dried and allowed to cool under vacuum. THF was distilled under an atmosphere of dry nitrogen from sodium benzophenone ketyl. All other solvents were used as supplied (Analytical or HPLC grade), without prior purification. All organometallic reagents were used as supplied. Thin layer chromatography (TLC) was performed on aluminium or plastic sheets coated with 60 F_{254} silica. Sheets were visualised using iodine, UV light or 1% aqueous $KMnO_4$ solution. Flash chromatography was performed on Kieselgel 60 silica. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker DPX 400 (^{1}H: 400 MHz and ^{13}C: 100.6 MHz) spectrometer or a Bruker AC 200 (^{1}H: 200 MHz and ^{13}C: 50.3 MHz) spectrometer in the deuterated solvent stated. All chemical shifts (δ) are quoted in ppm and coupling constants (J) in Hz. Residual signals from the solvents were used as an internal reference. ^{13}C multiplicities were assigned using a DEPT sequence. Infrared spectra were recorded on a Perkin-Elmer 1750 IR Fourier Transform spectrophotometer using either films on NaCl plates (film) or KBr discs (KBr), while solution spectra were recorded in the solvent stated using 1.0 mm NaCl cells, with only the characteristic peaks quoted. Low resolution mass spectra (m/z) were recorded on VG MassLab 20–250 or Micromass Platform 1 spectrometers and high resolution mass spectra (HRMS) on a Micromass Autospec 500 OAT spectrometer. Techniques used were chemical ionisation (CI, NH_3), or atmospheric pressure chemical ionisation (APCI) using partial purification by HPLC with methanol–acetonitrile–water (40 : 40 : 20) as eluent. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter with a path length of 1 dm. Concentrations are quoted in g 100 mL^{-1}. Melting points were recorded on a Leica VMTG Galen III apparatus and are uncorrected. Elemental analyses were performed by the microanalysis service of either the Dyson Perrins Laboratory or the Inorganic Chemistry Laboratory, Oxford.

4,4-Dimethyloxazolidin-2-one **8**,[16] 5,5-dimethyloxazolidin-2-one **9**[17] and 3-(3′-phenylpropionyl)oxazolidin-2-one **10**[19] were prepared by the literature procedures.

Representative procedure 1

n-BuLi (1.1 eq.) was added to a stirred solution of the oxazolidin-2-one (1.0 eq.) in anhydrous THF at −78 °C. After 15 minutes, the acid chloride (1.3 eq.) was added dropwise *via* syringe and left at −78 °C for 30 minutes before being warmed to rt. After 2 hours, the reaction mixture was quenched with saturated aqueous NH_4Cl solution and acetic acid, extracted with EtOAc, washed sequentially with saturated aqueous $NaHCO_3$ solution and brine and dried over $MgSO_4$. The organic extracts were concentrated *in vacuo* and purified either by recrystallization (hexane–Et_2O) or by flash column chromatography on silica gel to give the required product.

Representative procedure 2

DIBAL (1 M in DCM, 2.0 eq.) was added dropwise to a stirred solution of the *N*-acyloxazolidin-2-one (1.0 eq.) in anhydrous DCM at −78 °C and stirred for 10 minutes. After quenching with saturated aqueous NH_4Cl solution at −78 °C, the resultant mixture was stirred at rt for 2 hours with Rochelles salt. The reaction mixture was extracted with DCM, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*.

Representative procedure 3

DIBAL (1 M in THF, 1.2 eq.) was added to a stirred solution of *N*-acyl-5,5-dimethyloxazolidin-2-one (1.0 eq.) in anhydrous THF at 0 °C. After 20 minutes, a solution of the lithiated phosphonate, prepared by addition of *n*-BuLi (2.5 eq.) to a solution of phosphonate (2.5 eq.) in anhydrous THF at −78 °C and stirred for 30 minutes, was added *via* cannula. The reaction mixture was warmed to rt and stirred for 1 hour. After quenching with water at −78 °C, addition of Rochelles salt solution and stirring for 2 hours, the reaction mixture was extracted with EtOAc, washed with brine, dried with $MgSO_4$ and concentrated *in vacuo* before purification by flash column chromatography on silica gel.

Representative procedure 4

LHMDS (1.5 eq.) was added to a stirred solution of *N*-acyl-5,5-dimethyloxazolidin-2-one (1.0 eq.) in anhydrous THF at 0 °C. After stirring at 0 °C for 1 hour, the alkyl halide (3.0 eq.) was added *via* syringe. After 4 hours, the reaction was quenched with saturated aqueous NH_4Cl solution at 0 °C. The reaction mixture was extracted with EtOAc, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* before purification by flash column chromatography on silica gel.

Preparation of 3-(3′-phenylpropionyl)-4,4-dimethyloxazolidin-2-one 11

Following representative procedure 1, *n*-BuLi (1.66 M, 4.44 mL, 7.10 mmol), **8** (0.74 g, 6.45 mmol) and hydrocinnamoyl chloride (1.25 mL, 8.39 mmol) gave, after purification by flash column chromatography on silica (3 : 2 Et_2O–40–60 petroleum; R_f 0.43) and recrystallisation (hexane–Et_2O), **11** as white crystals (1.19 g, 75%); mp 45–46 °C (hexane–Et_2O); $C_{14}H_{17}NO_3$ requires C 68.0, H 6.9, N 5.7%, found C 68.0, H 6.9, N 5.7%; ν_{max} (film) 1777 (C=O endocyclic), 1703 (C=O exocyclic); δ_H (400 MHz, $CDCl_3$) 1.56 (6H, s, C(C*H*$_3$)$_2$), 2.97 (2H, t, *J* 7.7, CH_2C*H*$_2$Ph), 3.20 (2H, t, *J* 7.7, C*H*$_2$$CH_2$Ph), 3.99 (2H, s, OC*H*$_2$), 7.19–7.31 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.8 (C(*C*H$_3$)$_2$), 30.4 (Ph*C*H$_2$), 38.5 (PhCH_2*C*H$_2$), 60.4 (O*C*H$_2$), 75.2 (*C*Me$_2$), 126.2 (Ph_{para}), 128.4, 128.5 (Ph_{meta}, Ph_{ortho}), 140.6 (Ph_{ipso}), 154.1 (*C*ON), 173.4 (O*C*ON); *m*/*z* (APCI$^+$) 248.1 (MH$^+$, 10%).

Preparation of 3-(3′-phenylpropionyl)-5,5-dimethyloxazolidin-2-one 12

Following Representative Procedure 1, *n*-BuLi (2.5 M, 2.0 mL, 4.77 mmol), **9** (0.50 g, 6.45 mmol) and hydrocinnamoyl chloride (0.84 mL, 5.64 mmol) gave, after recrystallisation (EtOAc–hexane) **12** as a white solid (0.90 g, 84%); mp 71 °C (EtOAc–hexane); $C_{14}H_{17}NO_3$ requires C 68.0, H 6.9, N 5.7%, found C 68.4, H 6.8, N 5.4%; ν_{max} (film) 1757 (C=O endocyclic), 1697 (C=O exocyclic); δ_H (200 MHz; $CDCl_3$) 1.48 (6H, s, C(C*H*$_3$)$_2$), 2.99 (2H, t, *J* 7.6, PhC*H*$_2$), 3.28 (2H, t, *J* 7.6, PhCH_2C*H*$_2$), 3.74 (2H, s, C(4)*H*$_2$), 7.20–7.30 (5H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) 27.2 (C(*C*H$_3$)$_2$), 30.2 (Ph*C*H$_2$), 36.9 (PhCH_2*C*H$_2$), 54.3 (N*C*H$_2$), 78.7 (*C*Me$_2$), 126.4 (Ph_{para}), 128.7, 128.8 (Ph_{meta}, Ph_{ortho}), 140.8 (Ph_{ipso}), 152.8 (*C*ON), 173.2 (O*C*ON); *m*/*z* (APCI$^+$) 248.1 (MH$^+$, 20%).

Preparation of 3-(1′-hydroxy-3′-phenylpropyl)oxazolidin-2-one 13

Following Representative Procedure 2, DIBAL (1 M in DCM, 1.65 mL, 1.65 mmol) and **10** (180 mg, 0.82 mmol) furnished, after purification by flash column chromatography on silica (EtOAc–40:60 petrol 2 : 1), **13** (94 mg, 52%) as a white solid; mp 105 °C; ν_{max} (DCM) 1756 (C=O); δ_H (200 MHz, $CDCl_3$) 1.81–2.14 (2H, m, C(2′)*H*$_2$$CH_2$Ph), 2.57–2.87 (2H, m, CH_2C(3′)*H*$_2$Ph), 3.39 (1H, td, *J* 8.6, *J* 5.4, C(4)*H*$_A$H$_B$), 3.76 (1H, app q, *J* 8.6, C(4)H$_A$*H*$_B$), 4.14–4.38 (2H, m, C(5)*H*$_2$), 4.47 (1H, s, O*H*), 5.34 (1H, t, *J* 6.7, C(1′)*H*), 7.17–7.35 (5H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) 27.5 (*C(3′)*H$_2$), 28.1 (*C(2′)*H$_2$), 38.8 (*C(4)*H$_2$), 62.7 (*C(5)*H$_2$), 77.0 (*C(1′)*H), 126.3, 128.6 ($Ph_{ortho-,meta-,para-}$), 141.2 (Ph_{ipso}), 159.1 (O*C*ON); HRMS (CI$^+$) $C_{12}H_{14}NO_2$ (MH$^+$ − H_2O) requires 204.1024, found 204.1032.

DIBAL reduction of 3-(3′-phenylpropionyl)-4,4-dimethyloxazolidin-2-one 11

Following Representative Procedure 2, DIBAL (1 M in DCM, 1.62 mL, 1.62 mmol) and **11** (200 mg, 0.81 mmol) gave, after purification by repeated flash column chromatography on silica (hexane–EtOAc 7 : 1 increasing to 1 : 1, then 1.5 : 1) four major components identified as:

(i). Hydrocinnamaldehyde **15** (5 mg, 5%); δ_H (200 MHz, $CDCl_3$) 2.76–2.83 (2H, m, PhC*H*$_2$), 2.83–3.02 (2H, m, PhCH_2C*H*$_2$), 7.18–7.37 (5H, m, *Ph*), 9.84 (1H, s, C*H*O).[25]

(ii). Formic acid 2-methyl-2-(3′-phenylpropionyl amino)-propyl ester **17** (5 mg, 2%); R_f 0.53 (1.5 : 1 hexane–EtOAc); ν_{max} (film) 3326 (N–H), 1728 (C=O endocyclic), 1654 (C=O exocyclic); δ_H (400 MHz, $CDCl_3$) 1.30 (6H, s, NHC(C*H*$_3$)$_2$), 2.43 (2H, t, *J* 7.5, PhC*H*$_2$), 2.94 (2H, t, *J* 7.5, PhCH_2C*H*$_2$), 4.27 (2H, s, C*H*$_2$OCHO), 5.21 (1H, br s, N*H*), 7.19–7.31 (5H, m, *Ph*), 8.03 (1H, s, OC*H*O); δ_C (100 MHz, $CDCl_3$) 24.1 (C(*C*H$_3$)$_2$), 31.6 (Ph*C*H$_2$), 39.2 (PhCH_2*C*H$_2$), 53.0 (*C*Me$_2$), 68.1 (*C*H$_2$OCHO), 126.2 (Ph_{para}), 128.4, 128.5 (Ph_{meta}, Ph_{ortho}), 140.7 (Ph_{ipso}), 160.8 (*C*ONH), 171.8 (O*C*HO); HRMS (CI$^+$) $C_{14}H_{20}NO_3$ (MH$^+$) requires 250.1443, found 250.1450; *m*/*z* (APCI$^+$) 272.1 (MNa$^+$, 30%), 250.1 (MH$^+$, 100%).

(iii). 3-(1′-Hydroxy-3′-phenylpropyl)-4,4-dimethyloxazolidin-2-one **16** (48 mg, 24%); ν_{max} ($CHCl_3$) 3392 (O–H), 1737 (C=O); δ_H (400 MHz, $CDCl_3$) 1.25 (3H, s, C(C*H*$_3$)$_2$), 1.38 (3H, s, C(C*H*$_3$)$_2$), 2.18–2.27 (1H, m, C*H*$_A$H$_B$$CH_2$Ph), 2.42–2.51 (1H, m, CH$_A$*H*$_B$$CH_2$Ph), 2.65–2.82 (2H, m, CH_2C*H*$_2$Ph), 3.94 (1H, AB, *J* 8.3, OC*H*$_A$H$_B$), 4.01 (1H, AB, *J* 8.3, OCH$_A$*H*$_B$), 4.62 (1H, dd, $J_{1,OH}$ 6.1, $J_{1,2}$ 7.5, C*H*OH), 5.7 (1H, br s, O*H*), 7.18–7.31 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 25.6 (C*(C*H$_3$)$_2$), 27.5 (Ph*C*H$_2$), 28.1 (*C*H$_2$C(OH)), 59.1 (*C*Me$_2$), 75.3 (*C*H$_2$OCO), 77.6 (CH_2*C*(OH)), 126.0 (Ph_{para}), 128.4, 128.6 (Ph_{meta}, Ph_{ortho}), 140.8 (Ph_{ipso}), 157.3 (O*C*ON); HRMS (CI$^+$) $C_{14}H_{20}NO_3$ (MH$^+$) requires 250.1443, found 250.1444; *m*/*z* (APCI$^+$) 272.1 (MNa$^+$, 5%), 250.1 (MH$^+$, 10%).

(iv). 4,4-Dimethyloxazolidin-2-one **8** (22 mg, 24%).

Preparation of 3-(1′-hydroxy-3′-phenylpropyl)-5,5-dimethyloxazolidin-2-one 18

Following Representative Procedure 2, DIBAL (1 M in DCM, 4.05 mL, 4.05 mmol) and **12** (500 mg, 2.02 mmol) gave **18** as a white solid (490 mg, 98%). Purification by column chromatography on silica gel (EtOAc–40 : 60 petrol) gave **18** (370 mg, 74%); mp 96 °C; $C_{14}H_{19}NO_3$ requires C, 67.45, H, 7.7, N, 5.6%; found C 67.7, H, 7.8, N, 5.5%; ν_{max} (film) 1730 (C=O); δ_H (400 MHz, $CDCl_3$) 1.43 (3H, s, C(C*H*$_3$)$_2$), 1.47 (3H, s, C(C*H*$_3$)$_2$), 1.79–2.15 (2H, m, PhCH_2C*H*$_2$), 2.57–2.87 (2H, m, PhC*H*$_2$), 3.16 (1H, AB, *J* 8.4, NC*H*$_A$H$_B$), 3.52 (1H, AB, *J* 8.4, NCH$_A$*H*$_B$), 4.51 (1H, d, *J* 2.3, CHO*H*), 5.33–5.39 (1H, m, C*H*OH), 7.20–7.35 (5H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) 27.1 (C(*C*H$_3$)$_2$), 31.5 (Ph*C*H$_2$), 35.3 (*C*H$_2$C(OH)), 50.7 (N*C*H$_2$), 76.7 (CH_2*C*(OH)), 78.8 (*C*Me$_2$), 126.3, 128.7 ($Ph_{ortho-,meta-,para-}$), 141.3 (Ph_{ipso}), 158.2 (O*C*ON); *m*/*z* (APCI$^+$) 232.1 (MH$^+$ − H_2O, 10%).

Preparation of hydrocinnamaldehyde 15 from 12

DIBAL (1 M in DCM, 2 mL, 2 mmol) was added dropwise to a stirred solution of **12** (250 mg, 1.0 mmol) in anhydrous DCM at −78 °C and stirred for 10 minutes before the addition of saturated aqueous NH_4Cl (5 mL). After warming to rt, the reaction was extracted with DCM (3 × 25 mL), washed with brine, dried and concentrated *in vacuo*. To the residue was added $NaHSO_3$ (20 mmol in 10 mL H_2O) and the mixture stirred at rt and NaOH (1 M) was added until pH 9. After 3 hours the mixture was extracted with DCM (20 mL), HCl (1 M) was added to the aqueous layer until pH 1 and the products extracted with DCM (3 × 20 mL). The combined organic extracts were washed with saturated aqueous NH_4Cl, dried, and concentrated *in vacuo*. Purification by flash chromatography gave auxiliary **9** (90 mg, 78%) and hydrocinnamaldehyde **15** (122 mg, 91%).

Preparation of hydrocinnamaldehyde 15 from 18

(a). $NaHSO_3$ (20 mmol in 10 mL H_2O) and **18** (250 mg, 1.0 mmol) were stirred at rt and NaOH (1 M) was added until pH 9 and the reaction stirred for 6 hours before extraction with DCM (20 mL). HCl (1 M) was added to the aqueous layer until pH 1 and the products extracted with DCM (3 × 20 mL). The organic extracts were washed with saturated aqueous NH_4Cl, dried, and concentrated *in vacuo*. Purification by flash chromatography gave auxiliary **9** (83 mg, 75%) and hydrocinnamaldehyde **15** (120 mg, 90%).

(b). **18** (60 mg, 0.24 mmol) was added to a suspension of K_2CO_3 (47 mg, 0.34 mmol) in 4 : 1 MeOH–H_2O (10 mL) and stirred for 30 minutes before being partitioned with DCM (3 × 20 mL), washed with brine, dried, and concentrated *in vacuo*. Purification by flash chromatography gave auxiliary **9** (22 mg, 80%) and hydrocinnamaldehyde **15** (26 mg, 82%).

Preparation of (*E*)- and (*Z*)-ethyl 5-phenylpent-2-enoate 19 and 20 from 18

Following Representative Procedure 3, triethyl phosphonoacetate (0.32 mL, 1.61 mmol), *n*-BuLi (2.5 M, 0.63 mmol, 1.57 mmol) and **18** (200 mg, 0.80 mmol) in anhydrous THF (30 mL) gave, after purification by flash column chromatography on silica (30 : 1 hexane–Et_2O), (*Z*)-**20**[26] (36 mg, 22%); δ_H (400 MHz, $CDCl_3$) 1.29 (3H, t, *J* 7.2, $CO_2CH_2CH_3$), 2.78 (2H, t, *J* 7.7, C(5)H_2), 2.97–3.03 (2H, m, C(4)H_2), 4.17 (2H, q, *J* 7.1, CO_2CH_2Me), 5.79 (1H, dt, $J_{2,3}$ 11.4, $J_{2,4}$ 1.6, C(2)*H*), 6.25 (1H, dt, $J_{3,2}$ 11.4, $J_{3,4}$ 7.4, C(3)*H*), 7.18–7.31 (5H, m, *Ph*) and a more polar fraction (*E*)-**19**[26] (79 mg, 49%); δ_H (400 MHz, $CDCl_3$) 1.29 (3H, t, *J* 7.2, $CO_2CH_2CH_3$), 2.35–2.76 (4H, m, C(4)-H_2C(5)H_2Ph), 4.19 (2H, q, *J* 7.1, CO_2CH_2Me), 5.86 (1H, dt, $J_{2,3}$15.6, $J_{2,4}$1.4, C(2)*H*), 7.02 (1H, dt, $J_{3,2}$ 15.6, $J_{3,4}$ 6.8, C(3)*H*), 7.18–7.32 (5H, m, *Ph*). Further elution gave 5,5-dimethyloxazolidin-2-one **9** (65 mg, 70%).

Preparation of (*E*)- and (*Z*)-ethyl 5-phenylpent-2-enoate 19 and 20 from 12

Following Representative Procedure 3, DIBAL (1.0 M in THF, 0.73 mmol), **12** (150 mg, 0.61 mmol), *n*-BuLi (2.5 M, 0.49 mL, 1.22 mmol) and triethyl phosphonoacetate (0.25 mL, 1.22 mmol) in anhydrous THF (15 mL) gave a yellow oil. Purification by flash column chromatography on silica (30 : 1 hexane–Et_2O) furnished (*Z*)-**20** (11 mg, 9%) and (*E*)-**19** (76 mg, 61%).

Preparation of 3-butyroyl-5,5-dimethyloxazolidin-2-one 21

Following Representative Procedure 1, *n*-BuLi (2.5 M, 1.14 mL, 2.86 mmol), **9** (300 mg, 2.60 mmol) and butyryl chloride (0.35 mL, 3.38 mmol) gave, after purification by flash column chromatography on silica (5 : 1 hexane–Et_2O), **21** (420 mg, 88%) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.4, $CH_2CH_2CH_3$), 1.47 (6H, s, C(CH_3)$_2$), 1.63–1.68 (2H, m, CH_2-CH_2Me), 2.87 (2H, t, *J* 7.4, CH_2CH_2Me), 3.70 (2H, s, C(4)H_2); δ_C (100 MHz, $CDCl_3$) 13.6 ($CH_2CH_2CH_3$), 17.6 (CH_2CH_2Me), 27.2 (C(CH_3)$_2$), 37.1 (CH_2CH_2Me), 54.2 (*C*(4)H_2), 78.4 (*C*Me_2), 152.7 (O*C*N), 173.6 (O*C*ON); ν_{max} (film) 1778 (C=O endocyclic), 1702 (C=O exocyclic); *m*/*z* (APCI$^+$) 208.0 (MNH_4^+, 50%), 186.1 (MH^+, 100%); HRMS $C_9H_{16}NO_3$ (MH^+) requires 186.1130, found 186.1128.

Preparation of 3-pent-4′-enoyl-5,5-dimethyloxazolidin-2-one 22

Following Representative Procedure 1, *n*-BuLi (1.6 M, 1.8 mL, 2.87 mmol), **9** (300 mg, 2.61 mmol) and pent-4-enoyl chloride (770 mg, 6.53 mmol) gave, after purification by flash column chromatography on silica (2 : 1 hexane–Et_2O), **22** (498 mg, 97%) as a colourless oil; $C_{10}H_{15}NO_3$ requires C, 60.9, H, 7.7, N, 7.10%, found C, 60.9, H, 7.95, N, 6.9%; δ_H (400 MHz, $CDCl_3$) 1.48 (6H, s, C(CH_3)$_2$), 2.37–2.42 (2H, m, C(3′)H_2CH=CH_2), 3.02 (2H, t, *J* 7.4, C(2′)H_2), 3.71 (2H, s, C(4)H_2), 4.97–5.08 (2H, m, $J_{5',5'}$ 14.5; $J_{5',4'}$ 10.2, $J_{5',3'}$ 1.5, CH=C(5′)H_2), 5.80–5.84 (1H, m, C(4′)*H*=CH_2); δ_C (50 MHz, $CDCl_3$) 27.1 (C(CH_3)$_2$), 28.1 (*C*(3′)H_2), 34.5 (*C*(2′)H_2), 54.2 (*C*(4)H_2), 78.7 (*C*(5)Me_2), 115.8 (CH=*C*(5′)H_2), 137.0 (*C*(4′)H=CH_2), 153.0 (N*C*O), 173.3 (O*C*ON); ν_{max} (film) 1700 (C=O exocyclic), 1778 (C=O endocyclic), 1642 (C=C); *m*/*z* (APCI$^+$) 220.1 (MNa^+, 20%), 198.0 (MH^+, 15%).

Preparation of 3-(4′-methylpentanoyl)-5,5-dimethyloxazolidin-2-one 23

Following Representative Procedure 1, *n*-BuLi (1.66 M, 3 mL, 4.8 mmol), **9** (500 mg, 4.35 mmol) and 4-methylpentyl chloride (1.46 g, 10.9 mmol) gave, after purification by flash column chromatography on silica (3 : 1 hexane–Et_2O), **23** (577 mg, 62%) as a yellow solid; $C_{11}H_{19}NO_3$ requires C, 61.95, H, 9.0, N, 6.6%, found C, 62.15, H, 9.1, N, 6.50%; mp 31 °C; δ_H (400 MHz, $CDCl_3$) 0.92 (6H, d, *J* 6.4, C(4′)H(CH_3)$_2$), 1.50 (6H, s, C(5)Me_2), 1.52–1.64 (3H, m, C(3′)H_2C(4′)*H*Me_2), 2.93 (2H, m, C(2′)H_2), 3.73 (2H, s, C(4)H_2CMe_2); δ_C (50 MHz, $CDCl_3$) 22.1 (C(4′)H(CH_3)$_2$), 27.0 (C(CH_3)$_2$), 27.4 (*C*(4′)H), 32.9, 33.2 (*C*(2′)H_2, *C*(3′)H_2), 54.2 (*C*(4)H_2), 78.4 (*C*(5)Me_2), 152.9 (*C*ON), 174.2 (O*C*ON); ν_{max} (film) 1778 (C=O endocyclic), 1699 (C=O exocyclic); *m*/*z* (APCI$^+$) 236.1 (MNa^+, 25%), 214.1 (MH^+, 30%).

Preparation of 3-(3′,3′-dimethylbutyryl)-5,5-dimethyloxazolidin-2-one 24

Following Representative Procedure 1, *n*-BuLi (2.5 M, 0.77 mL, 1.91 mmol), **9** (200 mg, 1.74 mmol) and *tert*-butylacetyl chloride (0.40 mL, 2.26 mmol) gave, after recrystallization (hexane–Et_2O), **24** as a white solid (340 mg, 93%); $C_{11}H_{19}NO_3$ requires C, 61.95, H, 9.0, N, 6.6%, found C, 61.9, H, 8.7, N, 6.45%; mp 52–54 °C (hexane–Et_2O); δ_H (200 MHz, $CDCl_3$) 1.05 (9H, s, CH_2C(CH_3)$_3$), 1.48 (6H, s, C(CH_3)$_2$), 2.90 (2H, s, CH_2CMe_2), 3.72 (2H, s, $CH_2{}^t$Bu); δ_C (50 MHz, $CDCl_3$) 27.0 (C(CH_3)$_2$), 29.4 (CH_2C(CH_3)$_3$), 31.2 (CH_2CMe_3), 45.9 (CH_2CMe_2), 54.3 ($CH_2{}^t$Bu), 77.8 (*C*Me_2), 153.0 (O*C*N), 172.7 (O*C*ON); ν_{max} (KBr) 1760 (C=O endocyclic), 1692 (C=O exocyclic); *m*/*z* (APCI$^+$) 236.1 (MNa^+, 25%), 214.1 (MH^+, 45%).

Preparation of 3-(1′-hydroxybutyroyl)-5,5-dimethyloxazolidin-2-one 25

Following Representative Procedure 2, DIBAL (1 M in DCM, 2.2 mL, 2.2 mmol) and **21** (200 mg, 1.1 mmol) in anhydrous DCM (10 mL) gave **25** (190 mg, 94%) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.3, C(4′)H_3), 1.44, 1.47 (2 × 3H, s, C(CH_3)$_2$), 1.24–1.57 (3H, m, C(3′)H_A and C(2′)H_2), 1.64–1.73 (1H, m, C(3′)H_B), 3.19 (1H, d, *J* 8.5, C(4)H_A), 3.48 (1H, d, *J* 8.5, C(4)H_B), 4.27 (1H, d, *J* 3.8, O*H*), 5.30–5.35 (1H, m, C(1′)*H*OH); δ_C (100 MHz, $CDCl_3$) 13.7 (*C*(4′)H_3), 18.4 (*C*(3′)H_2), 27.2, 27.3 (C(CH_3)$_2$), 35.5 (*C*(2′)H_2), 50.8 (*C*(4)H_2), 76.7 (*C*(1′)H), 78.5 (*C*(5)Me_2), 157.8 (*C*=O); ν_{max} (film) 1741 (C=O); *m*/*z* (APCI$^+$) 187.2 (MH^+, 5%), 170.2 ($MH^+ - H_2O$, 100%); HRMS $C_9H_{15}NO_2$ ($MH^+ - H_2O$) requires 170.1181, found 170.1180.

Preparation of 3-(1′-hydroxy-3′,3′-dimethylbutyl)-5,5-dimethyloxazolidin-2-one 26

Following Representative Procedure 2, DIBAL (1 M in DCM, 1.9 mL, 1.9 mmol) and **24** (200 mg, 0.94 mmol) in anhydrous DCM (10 mL) gave **26** (120 mg, 60%) as white needles; mp 100–104 °C; δ_H (400 MHz, $CDCl_3$) 0.97 (9H, s, C(CH_3)$_3$), 1.42, 1.43 (2 × 3H, s, C(CH_3)$_2$), 1.43–1.49 (1H, m, C(2′)H_A), 1.59 (1H, dd,

$J_{2'B,2'A}$14.1, $J_{2'B,1'}$6.5, C(2′)H_B), 3.24 (1H, d, *J* 8.6, C(4)H_A), 3.50 (1H, d, *J* 8.6, C(4)H_B), 4.24 (1H, d, *J* 3.7, O*H*), 5.44–5.48 (1H, m, C(1′)*H*); δ_C (100 MHz, $CDCl_3$) 27.2, 27.3 (C(5)($CH_3)_2$), 29.6 (*C*(3′)), 29.8 (C(3′)($CH_3)_3$), 46.6 (*C*(2′)H_2), 50.8 (*C*(4)H_2), 75.3 (*C*(1′)H), 78.5 (*C*(5)Me_2), 157.6 (OCON); ν_{max} (KBr) 3352 (O–H), 1732 (C=O); *m*/*z* ($APCI^+$) 170.0 (MH^+, 5%).

Preparation of (*E*)- and (*Z*)-ethyl hex-2-enoate 27 and 28 from 22

Following Representative Procedure 3, DIBAL (1.0 M in THF, 1.95 mL, 1.95 mmol), **22** (300 mg, 1.62 mmol), triethyl phosphonoacetate (0.81 mL, 4.05 mmol) and *n*-BuLi (2.5 M, 1.62 mL, 4.05 mmol) in anhydrous THF (20 mL) gave, after purification by flash column chromatography on silica (30 : 1 hexane–Et_2O), (*Z*)-**28**[27] (10 mg, 4%); δ_H (400 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.3, C(6)H_3), 1.30 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.43–1.54 (2H, m, C(5)H_2), 2.61–2.67 (2H, m, C(4)H_2), 4.17 (2H, q, *J* 7.1, $CO_2CH_2CH_3$), 5.78 (1H, dt, $J_{2,3}$10.0, $J_{2,4}$1.7, C(2)*H*), 6.23 (1H, dt, $J_{2,1}$11.5, $J_{2,3}$7.5, C(3)*H*). Further elution gave (*E*)-**27**[27] (92 mg, 40%); δ_H (400 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.4, C(6)H_3), 1.29 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.45–1.54 (2H, m, C(5)H_2), 2.15–2.21 (2H, m, C(4)H_2), 4.19 (2H, q, *J* 7.1, CO_2CH_2Me), 5.82 (1H, dt, $J_{2,3}$ 15.6, $J_{2,4}$ 1.5, C(2)*H*), 6.97 (1H, dt, $J_{3,2}$ 15.6, $J_{3,4}$ 7.0, C(3)*H*). Further elution gave 5,5-dimethyl-oxazolidin-2-one **9** (55 mg, 0.48 mmol, 56%).

Preparation of (*E*)- and (*Z*)-ethyl hepta-2,6-dienoate 29 and 30 from 22

Following Representative Procedure 3, DIBAL (1.0 M in THF, 1 mL, 1.5 mmol), **22** (200 mg, 1.02 mmol), triethyl phosphono-acetate (0.51 mL, 2.54 mmol) and *n*-BuLi (1.66 M, 1.6 mL, 2.54 mmol) in anhydrous THF (15 mL) gave, after purification by flash column chromatography on silica (30 : 1 hexane–Et_2O), (*Z*)-**30** (12 mg, 8%); δ_H (400 MHz, $CDCl_3$) 1.30 (3H, t, *J* 7.2, $CO_2CH_2CH_3$), 2.21–2.43 (4H, m, CH_2CH_2CH=CH_2), 3.49 (2H, q, *J* 7.0, CO_2CH_2Me), 4.95–5.08 (2H, m, CH=CH_2), 5.77–5.86 (2H, m, *CH*=CH_2 and CH=*CH*CO_2Et), 6.22 (1H, dt, $J_{3,2}$ 11.5, $J_{3,4}$ 7.4, *CH*=CHCO_2Et). Further elution gave (*E*)-**29** (96 mg, 62%); δ_H (400 MHz, $CDCl_3$) 1.33 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 2.24–2.38 (4H, m, CH_2=CHCH_2CH_2), 4.23 (2H, q, *J* 7.1, CO_2CH_2Me), 5.04–5.13 (2H, m, CH_2=CH), 5.80–5.90 (2H, m, CH_2=*CH* and CH=*CH*CO_2Et), 7.00 (1H, dt, $J_{3,2}$15.6; $J_{3,4}$ 6.7, *CH*=CHCO_2Et); δ_C (100 MHz, $CDCl_3$) 22.6 ($CO_2CH_2CH_3$), 31.4, 32.0 (CH_2CH_2CH=CH_2), 60.2 (CO_2CH_2Me), 115.5 (CH=CH_2), 121.7 (*C*H=CH_2), 137.1 (CH=*C*HCO_2Et), 148.2 (*C*H=CHCO_2Et), 166.6 (CO_2Et); ν_{max} (film) 1716 (C=O), 1656 (C_2=C_3); HRMS $C_9H_{15}O_2$ (MH^+) requires 155.1072, found 155.1073; *m*/*z* ($APCI^+$) 155.1 (MH^+, 100%).

Preparation of (*E*)- and (*Z*)-ethyl 6-methylhept-2-enoate 31 and 32 from 23

Following Representative Procedure 3, DIBAL (1.0 M in THF, 1.41 mL, 1.41 mmol), **23** (200 mg, 0.94 mmol), triethyl phosphonoacetate (0.47 mL, 2.35 mmol) and *n*-BuLi (1.6 M, 1.47 mL, 2.35 mmol) in anhydrous THF (15 mL) gave, after purification by flash column chromatography on silica (30 : 1 hexane–Et_2O), (*Z*)-**32** (10 mg, 6%); δ_H (400 MHz, $CDCl_3$) 0.91 (6H, d, *J* 6.6, C(6)H($CH_3)_2$), 1.20–1.66 (6H, obscured m, $CO_2CH_2CH_3$, C(5)H_2CHMe_2 and CH_2C(6)*H*Me_2), 2.64–2.69 (2H, m, C(4)H_2CH_2CHMe_2), 4.18 (2H, q, *J* 7.1, CO_2CH_2Me), 5.75 (1H, dt, $J_{2,3}$11.5, $J_{2,4}$1.7, CH=C(2)*H*CO_2Et), 6.22 (1H, dt, $J_{3,2}$11.5, $J_{3,4}$7.6, C(3)*H*=CHCO_2Et). Further elution gave (*E*)-**31** (71 mg, 45%); δ_H (400 MHz, $CDCl_3$) 0.90 (6H, d, *J* 6.6, C(6)H($CH_3)_2$), 1.29 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.31–1.37 (2H, obscured m, C(5)H_2CHMe_2), 1.54–1.61 (1H, m, C(6)*H*Me_2), 2.17–2.23 (2H, m, C(4)H_2CH_2CHMe_2), 4.18 (2H, q, *J* 7.1, CO_2CH_2Me), 5.82 (1H, dt, $J_{2,3}$14.1, $J_{2,4}$1.5, CH=C(2)*H*CO_2Et), 6.97 (1H, dt, $J_{3,2}$ 15.6, $J_{3,4}$7.0, C(3)*H*=CHCO_2Et).

Preparation of (*E*)- and (*Z*)-ethyl 5,5-dimethylhex-2-enoate 33 and 34 from 24

Following Representative Procedure 3, DIBAL (1.0 M in THF, 1.69 mL, 1.69 mmol), **24** (300 mg, 1.41 mmol), triethyl phosphonoacetate (0.71 mL, 3.53 mmol) and *n*-BuLi (2.5 M, 1.41 mL, 3.53 mmol) in anhydrous THF (20 mL) gave, after purification by flash column chromatography on silica (30 : 1 hexane–Et_2O), (*Z*)-**34**[28] (11 mg, 7%); δ_H (500 MHz, $CDCl_3$) 0.95 (9H, s, C($CH_3)_3$), 1.25 (3H, t, *J* 7.2, $CO_2CH_2CH_3$), 2.59 (2H, dd, $J_{4,3}$7.8, $J_{4,2}$1.2, C(4)H_2), 4.16 (2H, q, *J* 7.2, CO_2CH_2Me), 5.84 (1H, dt, $J_{2,3}$ 11.6, $J_{2,4}$ 1.7, C(2)*H*), 6.29 (1H, dt, $J_{3,2}$ 11.6, $J_{3,4}$ 7.8, C(3)*H*). Further elution gave polar fraction (*E*)-**33**[28] (90 mg, 36%); δ_H (500 MHz, $CDCl_3$) 0.93 (9H, s, C($CH_3)_3$), 1.29 (3H, t, *J* 7.2, $CO_2CH_2CH_3$), 2.08 (2H, dd, $J_{4,3}$ 6.6, $J_{4,2}$ 1.2, C(4)H_2), 4.18 (2H, q, *J* 7.2, CO_2CH_2Me), 5.80 (1H, dt, $J_{2,3}$ 15.5, $J_{2,4}$ 1.2, C(2)*H*), 6.98 (1H, dt, $J_{3,2}$ 15.5, $J_{3,4}$ 7.8, C(3)*H*).

Preparation of (*E*)- and (*Z*)-*tert*-butyl hex-2-enoate 35 and 36 from 21

Following Representative Procedure 3, DIBAL (1.0 M in THF, 1.95 mL, 1.95 mmol), **21** (300 mg, 1.15 mmol), *tert*-butyl di-methoxyphosphonoacetate (910 mg, 4.05 mmol) and *n*-BuLi (1.6 M, 2.6 mL, 4.05 mmol) in anhydrous THF (20 mL) gave, after purification by flash column chromatography on silica (150 : 1 hexane–Et_2O) (*Z*)-**36**[29] (56 mg, 20%); δ_H (400 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.4, $CH_2CH_2CH_3$), 1.49 (9H, s, C($CH_3)_3$), 1.40–1.57 (2H, obscured m, CH_2CH_2Me), 2.56–2.62 (2H, m, CH_2CH_2Me), 5.69 (1H, d, $J_{2,3}$1.6, CH=*CH*$CO_2{}^t$Bu), 6.12 (1H, dt, $J_{3,2}$ 11.6, $J_{3,4}$ 7.5, *CH*=CH$CO_2{}^t$Bu). Further elution gave (*E*)-**35** (210 mg, 76%); δ_H (400 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.4, $CH_2CH_2CH_3$), 1.20–1.40 (2H, m, CH_2CH_2Me), 1.49 (9H, s, C($CH_3)_3$), 2.13–2.18 (2H, m, CH_2CH_2Me), 5.74 (1H, dt, $J_{2,3}$ 12.6, $J_{2,4}$1.5, CH=*CH*$CO_2{}^t$Bu), 6.86 (1H, dt, $J_{3,2}$15.6, $J_{3,4}$7.0, *CH*=CH$CO_2{}^t$Bu).

Preparation of 3-(2′-benzylpropionyl)-5,5-dimethyloxazolidin-2-one 37

Following Representative Procedure 4, LHMDS (1 M, 1.21 mL, 1.21 mmol), **12** (200 mg, 0.81 mmol) and MeI (0.15 mL, 2.43 mmol) in anhydrous THF (10 mL) gave, after purification by flash column chromatography on silica (2 : 1 40–60 petrol–EtOAc), **37** (190 mg, 90%) as a colourless oil; ν_{max} (film) 1783 (C=O endocyclic), 1703 (C=O exocyclic); δ_H (200 MHz, $CDCl_3$) 1.19 (3H, d, *J* 6.8, C(3′)H_3), 1.34, 1.43 (2 × 3H, s, C($CH_3)_2$), 2.67 (1H, dd, $J_{A,B}$13.2, $J_{A,2'}$7.7, CH_AH_BPh), 3.04 (1H, dd, $J_{B,A}$13.2, $J_{B,2'}$7.3, CH_AH_BPh), 3.58–3.72 (2H, m, C(4)H_2), 4.09–4.20 (1H, m, C(2′)*H*), 7.16–7.32 (5H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) 16.7 (*C*(3′)H_3), 26.9, 27.0 (C($CH_3)_2$), 39.3 (*C*(2′)H), 40.0 (C(2′)CH_2Ph), 54.4 (*C*(4)H_2), 78.3 (*C*(5)), 126.3, 128.1, 128.3 ($Ph_{ortho-,meta-,para-}$), 139.2 (Ph_{ipso}), 152.3 (CO), 176.8 (OCON); HRMS ($APCI^+$), $C_{15}H_{20}NO_3$ requires 262.1443, found 262.1448.

Preparation of 3-(2′-benzylpent-4′-enoyl)-5,5-dimethyloxazol-idin-2-one 38

Following Representative Procedure 4, LHMDS (1.0 M, 3.0 mL, 3.0 mmol), **12** (0.50 g, 2.02 mmol) and allyl bromide (0.53 mL, 6.07 mmol) in anhydrous THF (25 mL) gave **38** as a yellow solid (0.47 g, 1.65 mmol, 82%) after purification by flash column chromatography on silica (3 : 1 hexane–Et_2O; R_f 0.33); mp 53–55 °C; δ_H (400 MHz, $CDCl_3$) 1.25 (3H, s, C($CH_3)_2$), 1.43 (3H, s, C($CH_3)_2$), 2.28–2.34 (1H, m, CH_AH_BCH=CH_2), 2.44–2.51 (1H, m, CH_AH_BCH=CH_2), 2.8 (1H, dd, $J_{A,B}$13.4, $J_{A,2}$6.6, CH_AH_BPh), 2.96 (1H, dd, $J_{B,A}$13.4, $J_{B,2}$ 8.7, CH_AH_BPh), 3.58 (2H, ABq, *J* 11.0, CH_2CMe_2), 4.34–4.12 (1H, m, *CH*CH_2-CH=CH_2), 5.01–5.10 (2H, m, CH=CH_2), 5.76–5.86 (1H, m, *CH*=CH_2), 7.16–7.28 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$)

26.7, 26.9 (C(CH_3)$_2$), 36.3 (CH_2Ph), 38.3 (CH_2CH=CH$_2$), 44.1 (CHCH$_2$CH=CH$_2$), 54.3 (CH_2CMe$_2$), 78.3 (CMe$_2$), 117.3 (CH=CH$_2$), 126.6 (Ph_{para}), 128.6, 129.3 (Ph_{meta}, Ph_{ortho}), 135.5 (CH=CH$_2$), 139.2 (Ph_{ipso}), 152.6 (NCO), 176.1 (OCON); ν_{max} (KBr disc) 1771 (C=O endocyclic), 1693 (C=O exocyclic), 1639 (C=C); HRMS $C_{17}H_{22}NO_3$ (MH^+) requires 288.1600, found 288.1602; *m*/*z* ($APCI^+$) 310.2 (MNa^+, 30%), 288.2 (MH^+, 40%).

Preparation of 3-(1′-hydroxy-2′-benzylpropyl)-5,5-dimethyl-oxazolidin-2-ones 39 and 40

Following Representative Procedure 2, DIBAL (1 M in DCM, 1.15 mmol) and **37** (150 mg, 0.56 mmol) in anhydrous DCM (7 mL) gave, after purification by flash column chromatography (5 : 1 hexane–Et$_2$O) **39**–**40** (112 mg, 76%) as a colourless oil and a 3 : 1 mixture of diastereoisomers; Found C, 68.3, H, 8.2, N, 5.1%; $C_{15}H_{21}NO_3$ requires C, 68.4, H, 8.0, N, 5.3%; *m*/*z* ($APCI^+$) 246 ($MH^+ - H_2O$); ν_{max} (DCM) 1754 (C=O); Data for major diastereoisomer; δ_H (400 MHz, CDCl$_3$) 0.78 (3H, d, *J* 6.8, C(3′)H_3), 1.45, 1.49 (2 × 3H, s, C(CH_3)$_2$), 1.95–2.05 (1H, m, C(2′)H), 2.33–2.41 (1H, obscured m, CH_AH$_B$Ph), 3.18 (1H, d, *J* 8.6, C(4)H_A), 3.2 (1H, dd, $J_{B,A}$13.6, $J_{B,2'}$3.7, CH$_A$$H_B$Ph), 3.56 (1H, d, *J* 8.6, C(4)H_B), 4.31 (1H, d, *J* 3.8, OH), 5.03–5.10 (1H, obscured m, CHOH), 7.14–7.39 (5H, m, *Ph*); δ_C (50 MHz, CDCl$_3$) 14.3 (C(3′)H$_3$), 27.1, 27.3 (C(CH_3)$_2$), 38.4 (C(2′)H), 38.8 (C(2′)CH$_2$Ph), 50.9 (C(4)H$_2$), 78.7 (C(5)), 81.0 (C(1′)), 126.1, 128.5, 129.7 ($Ph_{ortho-,meta-,para-}$), 140.4 (Ph_{ipso}), 158.5 (C=O); Data for minor diastereoisomer; δ_H (400 MHz, CDCl$_3$) 1.02 (3H, d, *J* 6.6, C(3′)H_3), 1.40, 1.48 (2 × 3H, s, C(CH_3)$_2$), 1.95–2.05 (1H, m, C(2′)H), 2.33–2.41 (1H, obscured m, CH_AH$_B$Ph), 2.75 (1H, dd, $J_{B,A}$ 13.7, $J_{B,2'}$ 4.5, CH$_A$$H_B$Ph), 3.13 (1H, d, *J* 8.6, C(4)H_A), 3.55 (1H, d, *J* 8.6, C(4)H_B), 4.26 (1H, d, *J* 3.9, OH), 5.03–5.10 (1H, obscured m, CH), 7.14–7.39 (5H, m, *Ph*); δ_C (50 MHz, CDCl$_3$) 15.9 (C(3′)H$_3$), 27.1, 27.3 (C(CH_3)$_2$), 38.4 (C(2′)H), 38.9 (C(2′)CH$_2$Ph), 51.1 (C(4)H$_2$), 78.7 (C(5)), 81.3 (C(1′)), 126.3, 128.6, 129.3 ($Ph_{ortho-,meta-,para-}$), 140.2 (Ph_{ipso}), 158.5 (C=O).

Preparation of 2-benzylpropionaldehyde 41 from 39–40

NaHSO$_3$ (23.2 mmol in 15 mL H$_2$O) and **39**–**40** (304 mg, 1.16 mmol) were stirred at rt and NaOH (1 M) was added until pH 9 and the reaction stirred for 6 hours before extraction with DCM (20 mL). HCl (1 M) was added to the aqueous layer until pH 1 and the products extracted with DCM (3 × 20 mL) and the combined organic extracts were washed with saturated aqueous NH$_4$Cl, dried, and concentrated *in vacuo*. Purification by flash chromatography gave auxiliary **9** (107 mg, 81%) and **41** (155 mg, 91%).

Preparation of 2-benzylpropionaldehyde 41 from 37

DIBAL (1 M in DCM, 3.07 mL, 3.07 mmol) was added dropwise to a stirred solution of **37** (400 mg, 1.53 mmol) in anhydrous DCM (15 mL) at −78 °C and stirred for 10 minutes before the addition of saturated aqueous NH$_4$Cl (5 mL). After warming to rt, the reaction was extracted with DCM (3 × 25 mL), washed with brine, dried and concentrated *in vacuo*. To the residue was added NaHSO$_3$ (30.7 mmol in 10 mL H$_2$O) and the mixture stirred at rt and NaOH (1 M) was added until pH 9. After 3 hours the mixture was extracted with DCM (20 mL), HCl (1 M) was added to the aqueous layer until pH 1 and the products extracted with DCM (3 × 20 mL). The combined organic extracts were washed with saturated aqueous NH$_4$Cl, dried, and concentrated *in vacuo*. Purification by flash chromatography gave auxiliary **9** (147 mg, 83%) and 2-benzylpropionaldehyde **41** (186 mg, 83%).

Preparation of ethyl (*E*)- and (*Z*)-4-methyl-5-phenylpent-2-enoate 42 and 43 from 37

Following Representative Procedure 3, DIBAL (1.0 M in THF, 1.38 mL, 1.38 mmol), **37** (300 mg, 1.15 mmol), triethyl phosphonoacetate (0.58 mL, 1.38 mmol) and *n*-BuLi (1.6 M, 1.8 mL, 2.88 mmol) in anhydrous THF (20 mL) gave, after purification by flash column chromatography on silica (30 : 1 hexane–Et$_2$O), (*Z*)-**43** (15 mg, 6%); δ_H (400 MHz, CDCl$_3$) 1.01 (3H, d, *J* 6.6, C(4)*Me*), 1.28 (3H, t, *J* 7.1, CO$_2$CH$_2$$CH_3$), 2.58 (1H, dd, $J_{A,B}$13.4, $J_{5,4}$7.6, C(5)H_A), 2.70 (1H, dd, $J_{B,A}$13.4, $J_{5,4}$6.8, C(5)H_B), 3.82–3.89 (1H, m, C(4)H), 4.14 (2H, q, *J* 7.1, CO$_2$$CH_2CH_3$), 5.69 (1H, d, *J* 11.5, C(2)H), 6.05 (1H, dd, $J_{3,2}$ 11.5, $J_{3,4}$ 10.1, C(3)H), 7.17–7.29 (5H, m, *Ph*); δ_C (100 MHz, CDCl$_3$) 14.2 (C(4)CH$_3$), 19.6 (CO$_2$CH$_2$$CH_3$), 34.3 ($C$(5)H$_2$Ph), 42.9 ($C$(4)H), 59.8 (CO$_2$$CH_2$Me), 76.7 ($C$(2)H), 118.6 ($C$(3)H), 125.9 ($Ph_{para}$), 128.1, 129.2 ($Ph_{meta}$, Ph_{ortho}), 139.8 (Ph_{ipso}), 154.9 (CO$_2$Et); ν_{max} (film) 1719 (C=O), 1651 (C=C); HRMS $C_{14}H_{19}O_2$ (MH^+) requires 219.1385, found 219.1380; *m*/*z* ($APCI^+$) 236.2 (MNH_4^+, 70%), 219.2 (MH^+, 100%). Further elution gave (*E*)-**42** (162 mg, 65%); δ_H (400 MHz, CDCl$_3$) 1.05 (3H, d, *J* 6.4, C(4)*Me*), 1.29 (3H, t, *J* 7.1, CO$_2$CH$_2$$CH_3$), 2.55–2.66 (1H, obscured m, C(5)H_A), 2.78 (1H, dd, $J_{A,B}$ 12.2, $J_{5,4}$ 5.5, C(5)H_B), 4.12–4.21 (1H, obscured m, C(4)H), 4.19 (2H, q, *J* 7.1, CO$_2$$CH_2$Me), 5.76 (1H, dd, $J_{2,3}$15.7, $J_{2,4}$1.0, C(2)H), 6.97 (1H, dd, $J_{3,2}$ 11.5, $J_{3,4}$ 7.0, C(3)H), 7.17–7.33 (5H, m, *Ph*); δ_C (100 MHz, CDCl$_3$) 14.2 (C(4)CH$_3$), 38.2 (CO$_2$CH$_2$$CH_3$), 42.3 ($C$(5)H$_2$), 60.2 (CO$_2$$CH_2$Me), 119.9 ($C$(3)H), 126.1 ($Ph_{para}$), 128.3, 128.5 ($Ph_{meta}$, Ph_{ortho}), 139.4 (Ph_{ipso}), 155.1 (C=O); ν_{max} (film) 1720 (C=O), 1651 (C=C); HRMS $C_{14}H_{19}O_2$ (MH^+) requires 219.1385, found 219.1380; *m*/*z* ($APCI^+$) 219.2 (MH^+, 100%).

Preparation of 3-(1′-hydroxy-2′-benzylpent-4′-enyl)-5,5-dimethyloxazolidin-2-ones 44 and 45

ZnCl$_2$ (1.0 M in Et$_2$O, 1.74 mL, 1.74 mmol) was added dropwise to a stirred solution of **38** (250 mg, 0.87 mmol) in anhydrous THF (10 mL) at −30 °C. After 30 minutes, DIBAL (1.0 M in THF, 1.74 mL, 1.74 mmol) was added and the reaction mixture stirred for a further hour. Following quenching with saturated aqueous NH$_4$Cl solution, the reaction mixture was stirred for 2 hours with Rochelles salt at rt, extracted with EtOAc, washed with brine and dried over MgSO$_4$. Concentration *in vacuo*, followed by purification by flash column chromatography on silica (1 : 1 hexane: Et$_2$O; R_f 0.32) furnished **44** and **45** as an inseparable 3 : 2 mixture of diastereoisomers (230 mg, 92%); mp 79–82 °C; ν_{max} (KBr) 3341 (OH), 1717 (C=O); HRMS $C_{17}H_{22}NO_2$ ($MH^+ - H_2O$) requires 272.1651; found 272.1651; *m*/*z* ($APCI^+$) 272.2 ($MH^+ - H_2O$, 100%); δ_H (400 MHz, CDCl$_3$) {Major diastereoisomer} 1.46 and 1.49 (2 × 3H, s, C(CH_3)$_2$), 1.80 (1H, br s, OH), 2.25–2.33 (2H, m, CH_2CH=CH$_2$), 2.55–2.69 (obscured m, CH_AH$_B$Ph), 3.06 (1H, dd, $J_{A,B}$ 13.7, $J_{A,2'}$ 3.7, CH$_A$$H_B$Ph), 3.21 (1H, d, *J* 8.5, C(4)H_A), 3.57 (1H, d, *J* 8.5, C(4)H_B), 4.19 (1H, d, *J* 8.4, C(1′)H), 5.02–5.21 (obscured m, CH=CH_2 and CHCH=CH$_2$), 5.85–5.96 (1H, m, CH=CH$_2$), 7.15–7.31 (5H, m, *Ph*); δ_H (400 MHz, CDCl$_3$) {Minor diastereoisomer} 1.27, 1.43 (2 × 3Hs, C(CH_3)$_2$), 1.82 (1H, br s, OH), 1.96–2.18 (3H, m, CH_2CH=CH$_2$ and CH_AH$_B$Ph), 2.55–2.69 (1H, obscured m, CH$_A$$H_B$Ph), 2.86 (1H, d, *J* 8.5, C(4)H_A), 3.46 (1H, d, *J* 8.5, C(4)H_B), 4.19 (1H, d, *J* 8.4, C(1′)H), 5.02–5.21 (3H, obscured m, CH=CH_2 and CHCH=CH$_2$), 5.72–5.82 (1H, m, CH=CH$_2$), 7.15–7.31 (5H, m, *Ph*); δ_C (100 MHz, CDCl$_3$) 27.1, 27.3 (C(5)(CH_3)$_2$), 32.5, 33.7 (CH$_2$CH=CH$_2$), 34.9, 35.2 (CH$_2$Ph), 42.7, 42.9 (CHCH$_2$Ph), 50.9, 51.3 (C(4)H$_2$), 78.6 (C(5)Me$_2$), 79.1, 79.5 (C(1′)H), 117.7, 117.8 (CH=CH$_2$), 125.9, 126.0 (CH=CH$_2$), 128.3, 128.4, 128.9, 129.6 (Ph_{meta}, Ph_{ortho}), 135.0, 135.2 (Ph_{para}), 139.8, 140.1 (Ph_{ipso}), 158.1 (OCON).

Preparation of (*E*)- and (*Z*)-ethyl 4-benzylhepta-2,6-dienoate 46 and 47 from 44 and 45

Following Representative Procedure 3, triethyl phosphonoacetate (0.35 mL, 1.73 mmol), *n*-BuLi (1.6 M, 1.1 mL, 1.73 mmol) and **44** and **45** (200 mg, 0.69 mmol) gave, after purification by flash column chromatography on silica (30 : 1 40–60 petrol–Et_2O); (*Z*)-**47** (38 mg, 23%); δ_H (400 MHz, $CDCl_3$) 1.26 (3H, t, *J* 7.2, $CO_2CH_2CH_3$), 2.02–2.09 (1H, m, C(5)H_A), 2.21–2.28 (1H, m, C(5)H_B), 2.65 (1H, dd, $J_{A,B}$13.6, $J_{A,4}$7.3, CH_AH_B-Ph), 2.74 (1H, dd, $J_{B,A}$13.6, $J_{B,4}$7.0, CH_AH_BPh), 3.89–3.94 (1H, m, C(4)*H*), 4.13 (2H, q, *J* 7.2, CO_2CH_2Me), 5.00–5.05 (2H, m, C(7)H_2), 5.71–5.81 (2H, m, C(2)*H* and C(6)*H*), 6.00 (1H, dd, $J_{3,2}$ 11.6, $J_{3,4}$ 10.2, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 14.2 (CO_2-CH_2CH_3), 38.5, 38.9, 40.7 (*C*(5)H_2, CH_2Ph and *C*(4)H), 59.8 (CO_2CH_2Me), 116.4 (*C*(7)H_2), 120.0 (*C*(2)HCO_2Et), 126.0 (Ph_{para}), 128.1, 129.2 (Ph_{meta}, Ph_{ortho}), 136.1 (*C*(6)H), 139.6 (Ph_{ipso}), 153.0 (*C*(3)H), 166.2 (*C*O_2Et). Further elution gave (*E*)-**46** (97 mg, 58%); δ_H (400 MHz, $CDCl_3$) 1.28 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 2.11–2.29 (2H, m, $CH_2CH{=}CH_2$), 2.54–2.63 (1H, m, $CHCH_2CH{=}CH_2$), 2.66–2.80 (2H, m, CH_2Ph), 4.17 (2H, q, *J* 7.1, CO_2CH_2Me), 5.02–5.07 (2H, m, $CH{=}CH_2$), 5.68–5.79 (2H, m, $CH{=}CHCO_2$Et and $CH{=}CH_2$), 6.86 (1H, dd, $J_{3,2}$15.7, $J_{3,4}$8.4, $CH{=}CHCO_2$Et); δ_C (100 MHz, $CDCl_3$) 14.2 ($CO_2CH_2CH_3$), 37.8, 40.1, 43.7 ($CH_2CH{=}CH_2$, CH_2Ph and, $CHCH_2CH{=}CH_2$), 60.2 (CO_2CH_2Me), 117.1 ($CH{=}CH_2$), 121.5 ($CH{=}CHCO_2$Et), 126.2 (Ph_{para}), 128.3, 129.1 (Ph_{meta}, Ph_{ortho}), 135.5 ($CH{=}CH_2$), 139.3 (Ph_{ipso}), 151.5 ($CH{=}CHCO_2$Et), 166.5 (CO_2Et); ν_{max} (film) 1715 (C=O), 1654 (C=C); HRMS $C_{16}H_{21}O_2$ (MH^+) requires 245.1542, found 245.1538; *m*/*z* (APCI+) 262.2 (100%, MNH_3^+), 245.1 (100%, MH^+).

Formation of (*E*)- and (*Z*)-ethyl 4-benzylhepta-2,6-dienoate 46 and 47 from 38

$ZnCl_2$ (1.0 M in Et_2O, 1.4 mL, 1.40 mmol) was added to a stirred solution of **38** (200 mg, 0.70 mmol) in anhydrous THF (10 mL) at −30 °C. After 30 minutes, DIBAL (1.0 M in THF, 1.4 mL, 1.40 mmol) was added. After an additional hour, the phosphonate ylide {prepared from triethyl phosphonoacetate (0.35 mL, 1.75 mmol) and *n*-BuLi (1.6 M, 1.1 mL, 1.75 mmol) in THF (10 mL) at −78 °C for 30 minutes} was added and the reaction mixture warmed to rt. After two hours H_2O (20 mL) and a saturated solution of Rochelles salt (20 mL) were added. After stirring for 2 hours, the reaction mixture was extracted with EtOAc, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography on silica (40 : 1 40–60 petrol–Et_2O) gave (*Z*)-**47** (9 mg, 4%) and (*E*)-**46** (162 mg, 78%).

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