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Stereoselective synthesis of (*E*)-trisubstituted α,β-unsaturated amides and acids

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Potassium alkoxides of *N*-acyl-oxazolidin-2-one-*syn*-aldols undergo stereoselective elimination reactions to afford a range of trisubstituted (*E*)-α,β-unsaturated amides in >95% de, that may be subsequently converted into their corresponding (*E*)-α,β-unsaturated acids or (*E*)-α,β-unsaturated oxazolines in good yield. *syn*-Aldols derived from α,β-unsaturated aldehydes gave their corresponding trisubstituted (*E*)-α,β-unsaturated-amides with poorer levels of diastereocontrol, whilst there was a similar loss in (*E*)-selectivity during elimination of *syn*-aldols derived from chiral aldehydes. These elimination reactions proceed *via* rearrangement of the potassium alkoxide of the *syn*-aldol to a 1,3-oxazinane-2,4-dione enolate intermediate that subsequently eliminates carbon dioxide to afford a trisubstituted (*E*)-α,β-unsaturated amide. The (*E*)-selectivity observed during the E1cB-type elimination step has been rationalised using a simple conformational model that employs a chair-like transition state to explain the observed stereocontrol.

Introduction

(*E*)-2,3-Trisubstituted-α,β-unsaturated carboxylic acid derivatives are versatile synthetic fragments for natural product synthesis,[1] that also function as useful substrates for a wide range of asymmetric methodology.[2] They are most often prepared using highly stereoselective Wittig reactions, where reaction of an α-substituted-ester-ylid with an aldehyde affords the desired trisubstituted (*E*)-α,β-unsaturated ester in excellent yield.[3] Similar excellent levels of stereocontrol are also observed for Horner–Wadsworth–Emmons reactions, where anions of α-substituted-phosphonate esters also react with aldehydes in a highly (*E*)-selective manner.[4] Whilst less widely used in natural product synthesis, numerous other strategies have been developed for their stereoselective synthesis, including hydrocarboxylation of alkynes,[5] addition of carbanions to Baylis–Hillman adducts,[6] cross-metathesis approaches,[7] and the rearrangement of lithium ynolates.[8]

A wide range of aldol methodology is now available for the stereoselective synthesis of *syn*- or *anti*-α-alkyl-β-hydroxy-acid derivatives, and as a consequence, a number of elimination protocols has been developed for their stereoselective conversion into trisubstituted (*E*)-α,β-unsaturated acid derivatives. For example, Ohmizu *et al.* have shown that treatment of *anti*-α-alkyl-β-hydroxy-esters with EDCI and $CuCl_2$ in toluene at 80 °C results in *syn*-elimination to afford trisubstituted (*E*)-α,β-unsaturated esters, whilst treatment of the corresponding *syn*-α-alkyl-β-hydroxy-esters gave the alternative trisubstituted (*Z*)-α,β-unsaturated ester in high de.[9] Alternatively, treatment of α-alkyl-β-hydroxy-esters with excess triphenylphosphine and diethyl azodicarboxylate results in an *anti*-selective elimination reaction, with *syn*-α-alkyl-β-hydroxy-esters affording trisubstituted (*E*)-α,β-unsaturated esters, whilst *anti*-α-alkyl-β-hydroxy-esters gave their corresponding (*Z*)-isomers.[10] Bartoli *et al.* have reported that treatment of diastereoisomeric mixtures of *syn*-/*anti*-α-alkyl-β-hydroxy esters with $CeCl_3$ and NaI in refluxing acetonitrile gave trisubstituted (*E*)-esters in high de.[11] Similarly, Concellón *et al.* have described similar good levels of (*E*)-selectivity when samarium iodide is employed for the reductive elimination of mixtures of *syn*-/*anti*-α-halo-β-hydroxy-acid derivatives.[12] Mixtures of *syn*-/*anti*-α-alkyl-β-hydroxy-esters may also be dehydrated *via* step-wise protocols involving conversion to their corresponding tosylates/mesylates, followed by base-catalysed elimination to afford trisubstituted (*E*)-α,β-unsaturated esters in good de.[13] Only a few reports on the use of stereoselective versions of the Perkin reaction have been described, although Verkade *et al.* have described a potentially useful 'one-pot' protocol that employs a pro-azaphosphatrane base for the dehydrative aldol-condensation of an ester with an aldehyde to afford trisubstituted (*E*)-α,β-unsaturated esters in high de.[14]

Natural products that contain trisubstituted (*E*)-α,β-unsaturated-amide fragments also occur widely in nature,[15] whilst they have often been employed as structural motifs for the preparation of medicinally active compounds.[16] A number of different synthetic routes is available for their stereoselective synthesis, including direct amide formation from their corresponding (*E*)-acids[17] or (*E*)-esters,[18] Horner–Wadsworth–Emmons methodology,[19] aldol dehydration,[20] SmI_2 mediated elimination of α-chloro-β-hydroxy-amides or α,β-epoxy-amides,[21] or rearrangement of lithium ynolates.[22] The development of versatile protocols for their synthesis is therefore of great interest to the synthetic community. Consequently, we now report herein that potassium alkoxides of *N*-acyl-oxazolidin-2-one-*syn*-aldols undergo stereoselective elimination reactions to afford a highly practical route to trisubstituted (*E*)-α,β-unsaturated amides with good levels of stereocontrol. Part of this work has been communicated previously.[23]

Results and discussion

We have recently reported a novel aldol/cyclopropanation/*retro*-aldol strategy for the asymmetric synthesis of chiral cyclopropane carboxaldehydes in high de.[24] The success of this methodology required the development of conditions that would result in β-hydroxy-*N*-acyl-oxazolidin-2-ones undergoing a clean *retro*-aldol reaction to afford their respective *N*-acyl-oxazolidin-2-one and aldehyde fragments. In order to establish optimal conditions for this type of *retro*-aldol reaction, it was decided to employ a series of racemic β-hydroxy-*N*-acyl-oxazolidin-2-ones **3a–j** as simple model substrates to probe the steric and electronic requirements of this fragmentation pathway. Consequently, a series of four *N*-acyl-oxazolidin-2-ones **2a–d** were prepared in 62–74% yield *via* treatment of oxazolidin-2-one **1** in THF with 1.1 equivalents of *n*-BuLi at

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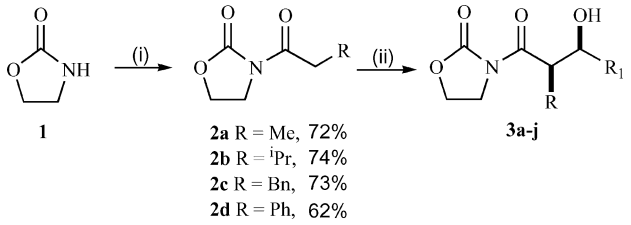
Table 1 Yields of *syn*-aldols **3a–j**

Aldol	R	R_1	de (%)	Yield (%)[a]
3a	^{i}Pr	Cyclohexyl	>95	58
3b	Me	Ph	>95	69
3c	Me	Et	>95	31
3d	Bn	$Me(CH_2)_6$–	>95	74
3e	^{i}Pr	Et	>95	48
3f	^{i}Pr	Ph	>95	50
3g	^{i}Pr	*p*$MeOC_6H_4$–	>95	60
3h	Ph	Et	>95	37
3i	^{i}Pr	(*E*)–MeCH=CH–	>95	72
3j	Me	(*E*)–PhCH=CH–	>95	88

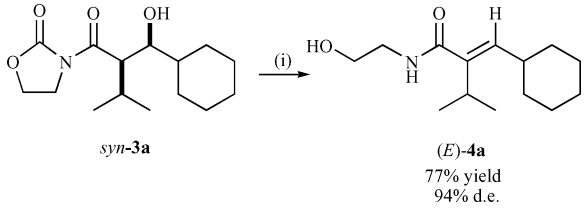
[a] Yields of *syn*-aldol products obtained in <70% were a result of unreacted *N*-acyl-oxazolidin-2-one **2a–d** being recovered at the end of the aldol reaction.

−78 °C, followed by addition of the appropriate acid chloride. After screening a range of boron sources and conditions, it was found that treatment of *N*-acyl-oxazolidin-2-ones **2a–d** with 9-BBN triflate (in hexanes) and $^i Pr_2NEt$ in CH_2Cl_2, followed by addition of the appropriate aldehyde at −78 °C, resulted in the formation of the desired *syn*-aldol products **3a–j**.[25] Examination of the ^{1}H NMR spectrum of each crude reaction product revealed the presence of desired *syn*-aldols **3a–j** in >95% de, which were purified to homogeneity by chromatography in poor to unoptimised 31–88% yields (Scheme 1, Table 1). The relative configuration of each of the racemic aldol products **3a–j** was assigned as *syn*- by analogy with literature precedent for the reaction of (*Z*)-boron-enolates of *N*-acyl-oxazolidin-2-ones in these types of aldol reactions.[26] This stereochemical assignment was subsequently confirmed for *syn*-aldol **3b** whose ^{1}H NMR spectrum was identical to the data previously reported for this diastereoisomer ($J_{(2,3)}$ = 3.0 Hz), whilst being clearly different from the ^{1}H NMR spectrum of its corresponding *anti*-aldol diastereoisomer ($J_{(2,3)}$ = 8.5 Hz).[27]



Scheme 1 *Reagents and conditions*: (i) *n*-BuLi, THF, −78 °C, RCH_2COCl; (ii) 9-BBN-OTf, $^i Pr_2NEt$, CH_2Cl_2, 0 to −78 °C, R_1CHO, CH_2Cl_2.

Attempts to establish anionic conditions that would result in *syn*-aldol **3a** undergoing a *retro*-aldol reaction under anionic conditions were unsuccessful, since treatment of *syn*-aldol **3a** with 1.5 equivalents of KHMDS in THF at −78 °C over a period of 2 hours resulted in an unexpected stereoselective elimination reaction to afford the trisubstituted α,β-unsaturated amide (*E*)-**4a** in 94% de, and in 77% isolated yield (Scheme 2). The geometry of the alkene functionality of (*E*)-**4a** was confirmed *via* X-ray crystallographic analysis that clearly revealed the *cis*-orientation of the α-iso-propyl group and the β-cyclohexane group (Fig. 1). Other aspects of the X-ray crystal structure of (*E*)-**4a** were



Scheme 2 *Reagents and conditions*: (i) KHMDS, THF, −78 °C.

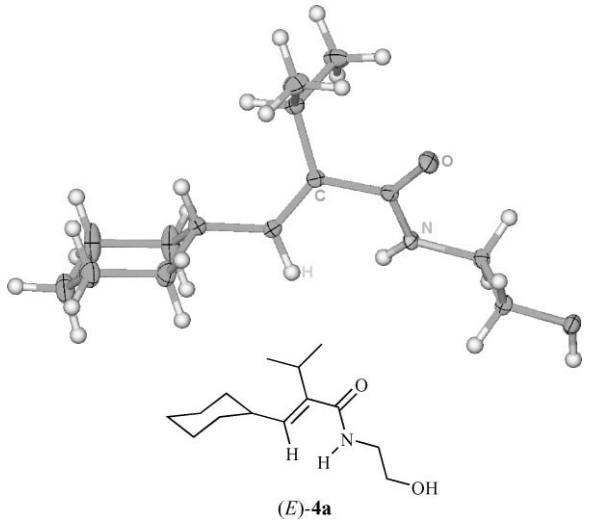
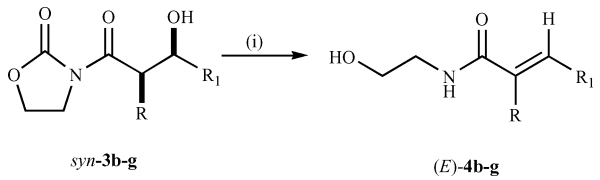


Fig. 1 One of the two molecules which comprise the asymmetric unit in the crystal structure of (*E*)-**4a**. Ellipsoids are depicted at the 30% probability level.

unremarkable, with crystal packing occurring *via* intermolecular hydrogen bonding between the primary hydroxyl groups of adjacent (*E*)-amide molecules.

In order to determine whether this elimination reaction was general in scope, the remaining series of *syn*-aldols **3b–g** was treated with 1.5 equivalents of KHMDS in THF at −78 °C for 2 hours, after which time the reaction was worked up with saturated $NH_4Cl_{(aq)}$. Examination of the crude ^{1}H NMR spectrum of each crude reaction product revealed that trisubstituted (*E*)-α,β-unsaturated amides **4b–g** had been formed in >90% de in each case, which were subsequently obtained in 67–99% yield after chromatographic purification (Scheme 3, Table 2). The structure of each (*E*)-α,β-unsaturated amide **4b–g** followed from comparison of their spectroscopic data with that of (*E*)-amide **4a**, whilst the alkene geometry of (*E*)-amides **4a–c** was confirmed *via* acidic hydrolysis to their known (*E*)-acids **26a–c** (*vide infra*). It is noteworthy that this simple elimination methodology appeared general in scope with linear and branched R substituents being tolerated at the α-position of *syn*-aldols **3a–g**, and with aliphatic and aromatic (neutral and electron rich) R_1-substituents being tolerated at their β-position (Scheme 1, Table 1). Attempts to carry out these elimination reactions at 0 °C resulted in the desired (*E*)-amides **4** being produced in inferior de; for example, treatment of *syn*-aldol **3b** with KHMDS in THF at 0 °C resulted in (*E*)-amide **4b** being produced in only 80% de.



Scheme 3 *Reagents and conditions*: (i) KHMDS, THF, −78 °C.

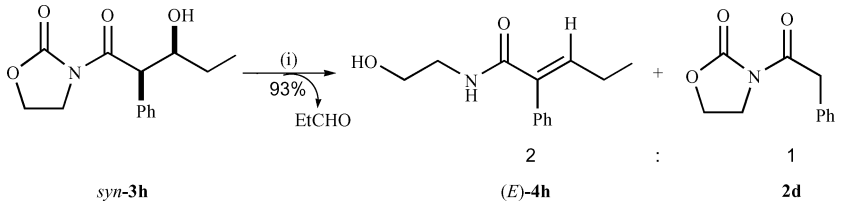
Table 2 Yields for synthesis of (*E*)-amides **4b–g**

Amide	R	R_1	de (%)	Yield (%)
4b	Me	Ph	>95	91
4c	Me	Et	>95	67
4d	Bn	$Me(CH_2)_6$–	92	91
4e	^{i}Pr	Et	>95	99
4f	^{i}Pr	Ph	92	90
4g	^{i}Pr	*p*$MeOC_6H_4$–	90	88

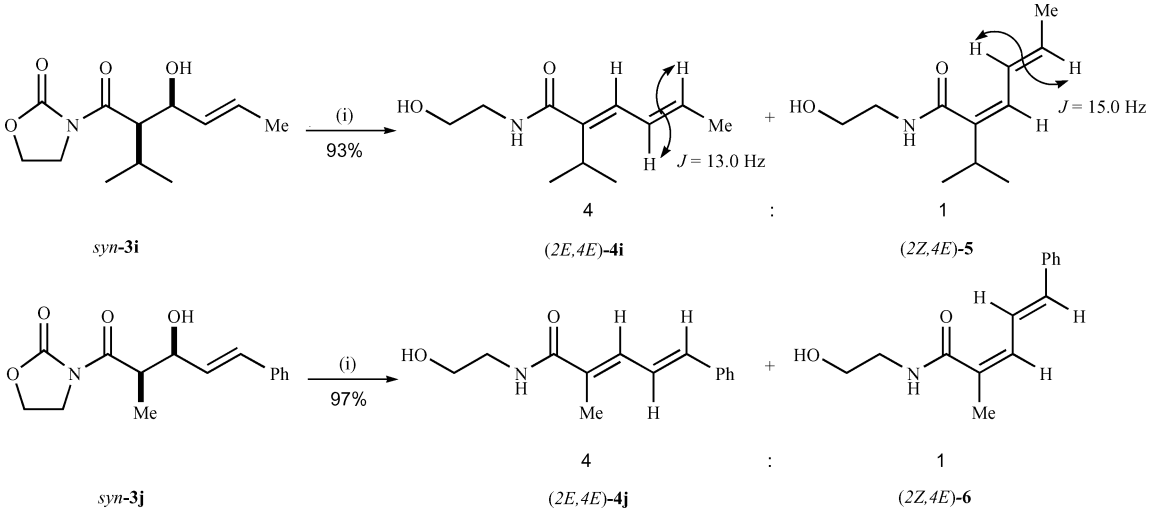
Further investigations revealed that elimination of *syn*-aldol **3h** containing an α-phenyl group under these conditions, gave a mixture of the desired (*E*)-amide **4h** (>95% de) and *N*-phenylacetyl-oxazolidin-2-one **2d** in a 2 : 1 ratio, which was purified by chromatography to afford (*E*)-**4h** in 47% yield. Presumably, *N*-phenylacetyl-oxazolidin-2-one **2d** arises from a competing *retro*-aldol reaction as originally conceived, where the potassium alkoxide of *syn*-aldol **3h** had fragmented to afford (*E*)-**4h** and propionaldehyde (not isolated). It is likely that the *retro*-aldol reaction of the alkoxide of *syn*-aldol **4h** is more favoured than for the other *syn*-aldols **4a–g** investigated in this study, because the enolate of *N*-phenylacetyloxazolidin-2-one **2d** is stabilised by the presence of its α-phenyl substituent (Scheme 4).

Treatment of *syn*-aldols **3i** and **3j** with KHMDS in CH_2Cl_2 at −78 °C afforded (2*E*,4*E*)-α,β,γ,δ-unsaturated amides **4i** and **4j** in a stereoselective manner, however they were both formed with poorer levels of stereocontrol. Thus, treatment of *syn*-aldol **3i** with KHMDS at −78 °C resulted in (2*E*,4*E*)-α,β,γ,δ-unsaturated amide **4i**, and its geometric isomer (2*Z*,4*E*)-α,β,γ,δ-unsaturated amide **5**, in a 4 : 1 ratio, and in a combined 93% yield (Scheme 5). Attempted chromatographic purification of these geometric isomers over silica gel was unsuccessful, however (2*E*,4*E*)-**4i** and (2*Z*,4*E*)-**5** could be partially separated *via* chromatography over silica gel doped with silver nitrate.[28] The presence of the (2*Z*)-alkene geometry of (2*Z*,4*E*)-**5** was confirmed from examination of its ^{1}H NMR spectrum which revealed a coupling constant of $J_{(4,5)} = 15.0$ Hz, that was similar in value to that observed for (2*E*,4*E*)-**4i** of $J_{(4,5)} = 13.0$ Hz. Similarly, treatment of *syn*-aldol **3j** with KHMDS in THF at −78 °C also gave a 4 : 1 mixture of (2*E*,4*E*)-**4j** and (2*Z*,4*E*)-**6** in a combined 97% yield (Scheme 5).[29] Fractional recrystallisation of this mixture of geometric isomers from ethyl acetate afforded the major amide (2*E*,4*E*)-**4j** in 64% isolated yield, whose alkene geometry was confirmed *via* hydrolysis to its known parent (2*E*,4*E*)-acid **27** (*vide infra*). Therefore, it appears that elimination of *syn*-aldols derived from α,β-unsaturated aldehydes under these conditions occurs with intrinsically poorer levels of stereocontrol than for the other *syn*-aldols **3a–g** investigated in this study.

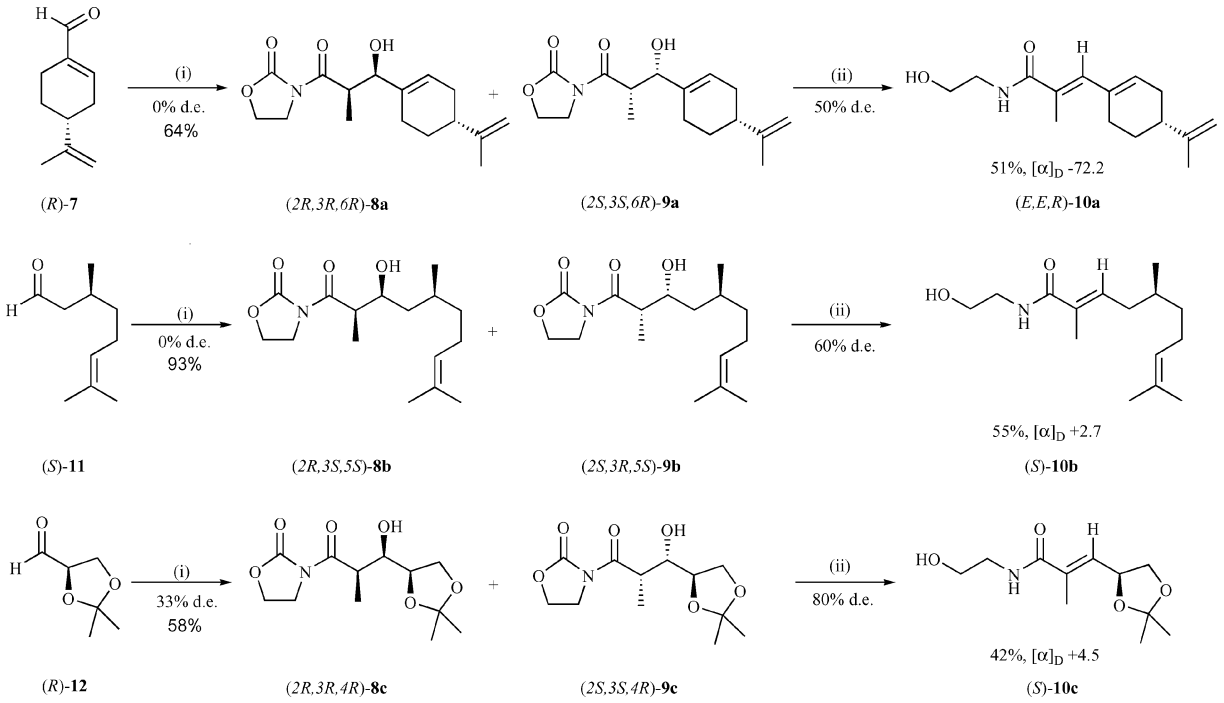
In order to demonstrate that this elimination methodology was applicable to the stereoselective synthesis of trisubstituted-(*E*)-amides of potential use as building blocks for natural product synthesis, we next explored its use for the preparation of three trisubstituted (*E*)-α,β-unsaturated amides **10a–c** derived from chiral aldehydes (Scheme 6). Reaction of the (*Z*)-boron enolate of *N*-propionyl-oxazolidin-2-one **2a** with perillaldehyde (*R*)-7 (90% pure) resulted in a 1 : 1 mixture of *syn*-aldol diastereoisomers **8a/9a** in 64% yield.[30] Treatment of this mixture of *syn*-aldols **8a/9a** with KHMDS in THF at −78 °C resulted in a clean elimination reaction to afford α,β,γ,δ-unsaturated amide (*E*,*E*,*R*)-**10a** in 50% de, which was purified to homogeneity *via* chromatography in 51% yield. Since elimination of *syn*-aldols derived from α,β-unsaturated aldehydes had been shown to afford (*E*,*E*)-unsaturated-amides in inferior de, we next reacted the (*Z*)-boron enolate of **2a** with citronellal (*S*)-**11** (96% pure) to afford an inseparable 1 : 1 mixture of diastereoisomeric *syn*-aldols **8b/9b** in 93% yield. This mixture was subsequently treated with KHMDS in THF at −78 °C to afford (*E*,*S*)-amide **10b** in 60% de, that was purified to homogeneity *via* chromatography in 55% yield. The moderate diastereocontrol observed in this elimination reaction was somewhat surprising, since elimination of the related *syn*-aldol **3d**, which also contained a long alkyl chain at its β-position, gave its corresponding (*E*)-amide **4d** in 92% de. Finally, reaction of the (*Z*)-boron enolate of **2a** with 1.1 equivalents of D-glyceraldehyde acetonide (*R*)-**12** afforded a 2 : 1 mixture of *syn*-aldol diastereoisomers **8c/9c** that were co-isolated in 58% yield after chromatography over silica.[31] The 2 : 1 mixture of *syn*-aldols **8c/9c** produced in this reaction is likely to result from attack of the boron-enolate of **2a** at the carbonyl of (*R*)-**12** occurring under substrate control, where formation of the major aldol diastereoisomer (stereochemistry not determined) is favoured by the stereodirecting effect of the α-stereogenic centre of aldehyde (*R*)-**12**. Generation of the potassium alkoxides of *syn*-aldols **8c/9c** *via* treatment of this mixture with KHMDS in THF at −78 °C, resulted in the formation of (*E*,*S*)-amide **10c** in 80% de, which was purified to homogeneity *via* chromatography in 42% isolated yield.[32]



Scheme 4 *Reagents and conditions*: (i) KHMDS, THF, −78 °C.



Scheme 5 *Reagents and conditions*: (i) KHMDS, THF, −78 °C.



Scheme 6 *Reagents and conditions*: (i) **2a**, 9-BBN-OTf, $^{i}Pr_2NEt$, CH_2Cl_2, 0 to −78 °C; (ii) KHMDS, THF, −78 °C.

Therefore, whilst the potassium alkoxides of *syn*-aldols **8a–c**/**9a–c** derived from chiral aldehydes eliminated to afford their desired trisubstituted α,β-unsaturated amides (*E*)-**10a–c**, it is clear that these reactions had proceeded with inferior levels of (*E*)-stereocontrol to those previously observed for the simpler *syn*-aldols **4a–g**.

Mechanism of the stereoselective elimination reaction of *syn*-aldols

It is well known that sterically unhindered *N*-acyloxazolidin-2-ones can undergo endocyclic ring cleavage *via* either inter- or intramolecular attack of alkoxide nucleophiles at their oxazolidin-2-one carbonyl groups.[33] Consequently, it was proposed that the high diastereoselectivities observed for the elimination of *syn*-aldols **3** could be explained by a novel intramolecular cyclisation/E1cB-type elimination mechanism as shown in Fig. 2. In this mechanism, deprotonation of *syn*-aldol **11** would result in potassium alkoxide **12**, that would then undergo intramolecular attack at the oxazolidin-2-one carbonyl resulting in *O–O* carbonyl migration to afford 1,3-oxazinane-2,4-dione alkoxide intermediate **13**. Subsequent anion equilibration of alkoxide **13** would then give 1,3-oxazinane-2,4-dione enolate **14** that would then undergo stereoselective elimination of carbon dioxide to afford the trisubstituted secondary amide (*E*)-**15** in high de (Fig. 2).

In order to provide evidence for this mechanism, it was proposed that treatment of 1,3-oxazinane-2,4-dione **16** with KHMDS in THF at −78 °C should result in stereoselective elimination to afford trisubstituted amide (*E*)-**4b** in an identical de to that observed for elimination of its parent *syn*-aldol **3b**. We have reported previously that zinc alkoxides of α-alkyl-β-hydroxy-*N*-acyl-oxazolidin-2-ones undergo clean rearrangement to afford 1,3-oxazinane-2,4-diones,[34] and as a consequence *syn*-1,3-oxazinane-2,4-dione **16** was prepared in 97% yield *via* treatment of *syn*-aldol **3b** with 10 mol% of Et_2Zn in CH_2Cl_2 at room temperature. Subsequent treatment of *syn*-1,3-oxazinane-2,4-dione **16** with KHMDS in THF at −78 °C gave amide (*E*)-**4b** in an identical >95% de to that previously observed for elimination of the potassium alkoxide of *syn*-aldol **3b** (Scheme 7).[35] This observation therefore provides good evidence that the potassium alkoxide of 1,3-oxazinane-2,4-diones **13**, and their corresponding enolates **14**, are key intermediates in these stereoselective elimination reactions (Fig. 2).

We next confirmed that the loss in stereoselectivity observed during elimination of the potassium alkoxides of *syn*-aldol **3i** was occurring during elimination of carbon dioxide from the enolate of *syn*-1,3-oxazinane-2,4-dione intermediate **17**. Thus, treatment of *syn*-aldol **3i** with 10 mol% Et_2Zn in CH_2Cl_2 resulted in a zinc alkoxide that cleanly rearranged to afford its *syn*-1,3-oxazinane-2,4-dione **17** in >95% de with no loss of stereochemical integrity at either its α- or β-stereocentres. *syn*-1,3-Oxazinane-2,4-dione **17** was treated with KHMDS in THF at −78 °C under conditions used previously for the direct elimination of *syn*-aldol **3i**, to afford an identical 4 : 1 ratio of (2*E*,4*E*)-α,β-unsaturated amide **4i** and (2*Z*,4*E*)-α,β-unsaturated amide **5** in an excellent 88% yield (Scheme 8). Therefore, it appears that the loss of stereocontrol observed for *syn*-aldol **3i** occurs exclusively during elimination of carbon dioxide from the enolate derived from *syn*-1,3-oxazinane-2,4-dione intermediate **17**.

Finally, we explored the elimination of the corresponding *anti*-aldol **18** which was prepared *via* treatment of **2a** with $MgCl_2$, TMSCl, Et_3N and benzaldehyde in EtOAc in an unoptimised 33% yield, according to Evans' recently published procedure.[36] Treatment of *anti*-aldol **18** with KHMDS in THF at −78 °C afforded amide (*E*)-**4b** in >95% de, a value identical to that

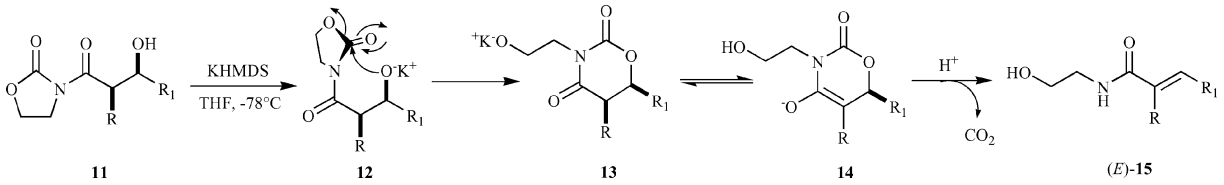
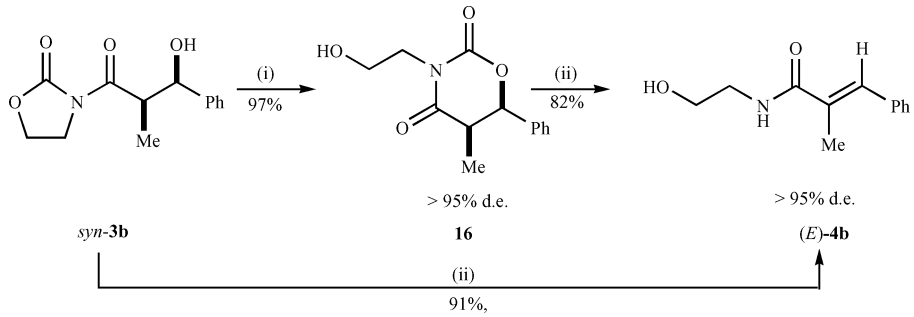
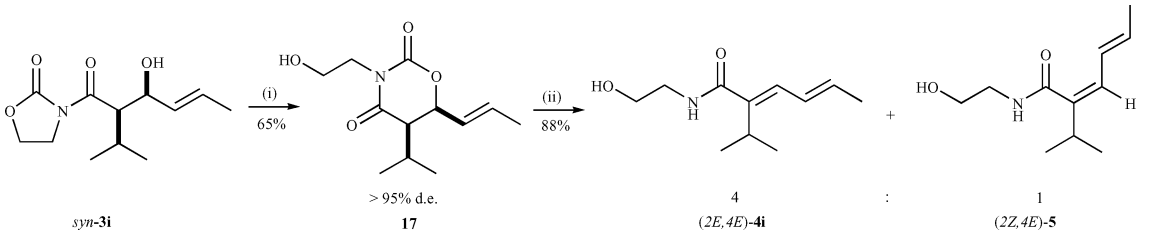


Fig. 2 Intramolecular cyclisation/E1cB-elimination mechanism for the stereoselective elimination of *syn*-aldol **11**.



Scheme 7 *Reagents and conditions*: (i) Et_2Zn, THF, rt; (ii) KHMDS, THF, −78 °C.



Scheme 8 *Reagents and conditions*: (i) 10 mol% Et_2Zn, THF, rt; (ii) KHMDS, THF, −78 °C.

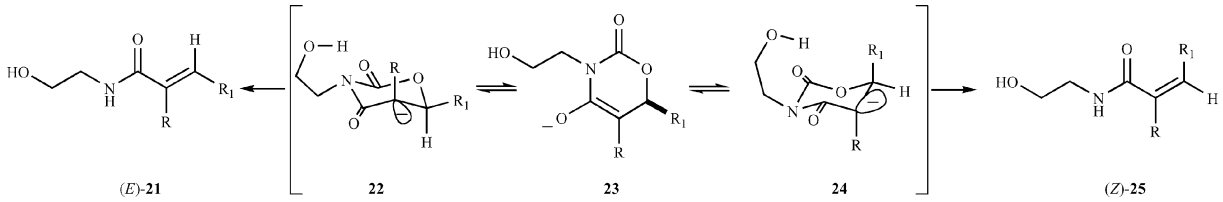
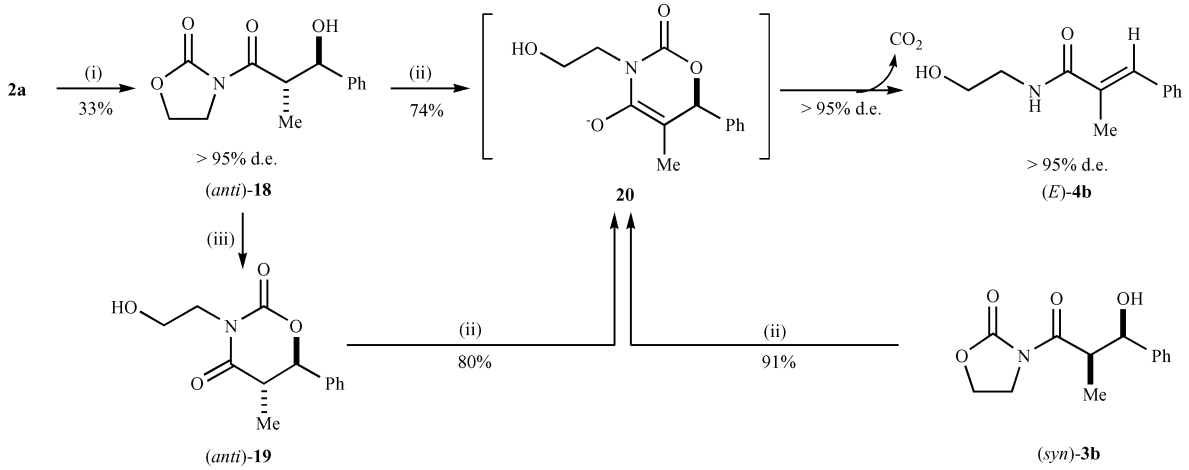


Fig. 3 Simple conformational model to explain (*E*)-selectivity in elimination reaction.

observed previously for elimination of the corresponding *syn*-aldol **3b** under the same conditions (Scheme 9). Furthermore, treatment of *anti*-aldol **18** with Et_2Zn in CH_2Cl_2 resulted in rearrangement to afford the corresponding *anti*-1,3-oxazinane-2,4-dione **19** in >95% de, which on treatment with KHMDS in THF at −78 °C also afforded amide (*E*)-**4b** in >95% de (Scheme 9). These observations are therefore clearly consistent with the key elimination step of both *anti*-aldol **18** and *syn*-aldol **3b** occurring *via* an E1cB-type mechanism, in which a common enolate intermediate **20** eliminates CO_2 to afford the α,β-unsaturated amide (*E*)-**4b** in high de (Scheme 9).

Whilst it is likely that the key E1cB-type elimination reactions of the 1,3-oxazinane-2,4-dione enolate **23** occur *via* a concerted reaction mechanism, the observed (*E*)-selectivity in these elimination reactions may be rationalised using a simple conformational model that compares the relative energies of transition state intermediates **22** and **24** (Fig. 3). In the case of transition state **22** that leads to (*E*)-amide **21**, concerted elimination of carbon dioxide from a cyclic ring system requires overlap of an equatorial C_5-carbanion with the *o**-orbital of the C_6–O bond, which can only occur from a chair conformer in which the C_5–R group occupies an axial position, and the C_6–R_1 group occupies an equatorial position. This compares with transition state **24** that leads to (*Z*)-amide **25**, where a similar orbital alignment results in a chair conformer in which both the C_5–R group and C_6–R_1 substituents both occupy axial positions. Since transition state **22** contains only one axial substituent, it is likely to be lower in energy than transition state **24** which contains two axial substituents, and as a consequence formation of (*E*)-amide **21** is favoured. Whilst this 'carbanion' model

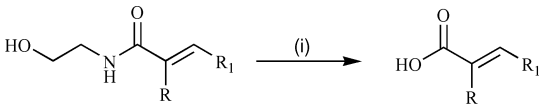


Scheme 9 *Reagents and conditions*: (i) $MgCl_2$, TMSCl, Et_3N, PhCHO, EtOAc; (ii) KHMDS, THF, −78 °C; (iii) 10 mol% Et_2Zn, THF, rt.

is clearly an over-simplification of the concerted elimination processes that are likely to be occurring in these elimination reactions, similar electronic and steric considerations are likely to be operating to maximise orbital overlap in the transition state that preferentially leads to the formation of (*E*)-amides in these reactions. However, it is also clear from the poorer levels of stereocontrol (50–80% de) observed for the elimination of *syn*-aldols derived from α,β-unsaturated aldehydes and chiral aldehydes, that subtle changes in the conformation and/or electron density of the transition states of these $E1_cB$-type reactions can result in significant losses in (*E*)-selectivity.

Synthesis of (*E*)-α,β-unsaturated carboxylic acids and (*E*)-α,β-unsaturated oxazolines

Having shown that this elimination methodology afforded an excellent general route to (*E*)-trisubstituted α,β-unsaturated amides, their conversion to other carboxylic acid derivatives was explored in order to demonstrate the synthetic versatility of this methodology. Five representative (*E*)-α,β-unsaturated amides **4a–d** and **4j** were refluxed in 6 M $HCl_{(aq)}$ for 5 hours to afford their corresponding (*E*)-α,β-unsaturated acids **26a–d** and **27** respectively in 77–99% isolated yield (Scheme 10, Table 3).[37] Importantly, examination of the ^{1}H NMR spectra of the crude reaction products of these hydrolysis reactions revealed that all of the α,β-unsaturated acids had been produced as single isomers with no evidence of any alkene migration having occurred under the strong acid conditions used for hydrolysis. The structures of α,β-unsaturated acids (*E*)-**26b** and (*E*)-**26c** were confirmed *via* comparison with commercially available samples of (*E*)-2-methylpentenoic acid and (*E*)-2-methyl-3-phenylpropenoic acid respectively, whilst spectroscopic data for (*E*)-**26a** and (*E*)-**27** were identical to previous literature reports.[38,39]



4a-d, 4j **26a-d, 27**

Scheme 10 *Reagents and conditions*: (i) 6 M $HCl_{(aq)}$.

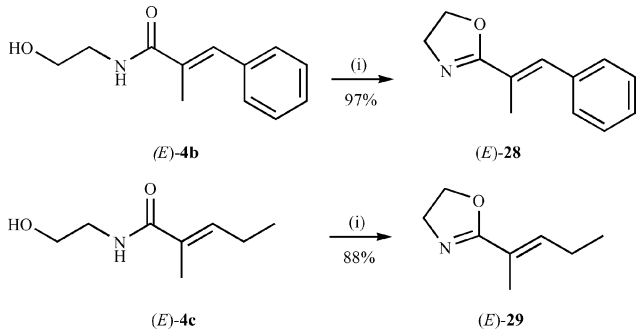
Table 3 Yields for synthesis of (*E*)-acids **26a–d** and **27**

Acid	R	R_1	de (%)	Yield (%)
26a	^{i}Pr	Cyclohexyl	>95	99
26b	Me	Ph	>95	95
26c	Me	Et	>95	91
26d	Bn	$Me(CH_2)_6$–	>95	95
27	Me	(*E*)–PhCH=CH–	>95	77

The synthetic potential of this methodology was further demonstrated *via* cyclisation of the *N*-hydroxyamide fragment of (*E*)-amides **4b** or **4c** to afford their corresponding trisubstituted (*E*)-α,β-unsaturated oxazolines (*E*)-**28** and (*E*)-**29**. Thus, addition of thionyl chloride (5 eq.) in a dropwise fashion to an ice-cold solution of α,β-unsaturated amides **4b** and **4c** in CH_2Cl_2, resulted in the desired oxazolines (*E*)-**28** and (*E*)-**29** in 97% and 88% yield respectively (Scheme 11). It should be noted that these types of (*E*)-α,β-unsaturated oxazolines are useful synthetic intermediates that are easily converted into their corresponding (*E*)-α,β-unsaturated acids, alcohols and aldehydes using known literature procedures.[40]

Conclusion

In conclusion, we have demonstrated that potassium alkoxides of *N*-acyl-oxazolidin-2-one derived-*syn*-aldols undergo stereoselective elimination reactions to afford a range of trisubstituted (*E*)-α,β-unsaturated amides in excellent de, that could be easily converted into their corresponding (*E*)-α,β-unsaturated acids or



Scheme 11 *Reagents and conditions*: (i) $SOCl_2$, CH_2Cl_2, 0 °C.

(*E*)-α,β-unsaturated oxazolines in good yield. Alkoxides of *syn*-aldols derived from α,β-unsaturated aldehydes were eliminated to afford their corresponding trisubstituted (*E*)-α,β-unsaturated-amides in an inferior 80% de, whilst there was also a similar loss in (*E*)-selectivity during elimination of more complex *syn*-aldols derived from chiral aldehydes. These elimination reactions proceed *via* rearrangement of their *syn*-aldol alkoxide to a 1,3-oxazinane-2,4-dione enolate intermediate that subsequently eliminates carbon dioxide to afford a trisubstituted (*E*)-α,β-unsaturated amide. The (*E*)-selectivity observed during the critical E1cB-type elimination step of this reaction has been rationalised using a simple conformational model that employs chair-like transition states to explain the observed stereocontrol.

Experimental

General experimental

All reactions were carried out under nitrogen or argon using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen. THF was distilled from sodium/benzophenone ketyl, whilst CH_2Cl_2 was distilled from CaH_2 under nitrogen. All other reagents were used as supplied without further purification. Flash column chromatography was performed on silica gel (Kieselgel 60). TLC was performed on Merck aluminium sheets coated with 0.2 mm silica gel 60 F254. Plates were visualised either by UV light (254 nm), iodine, ammonium molybdate (7% solution in ethanol) or potassium permanganate (1% in 2% aqueous acetic acid, containing 7% potassium carbonate). Infra red spectra were recorded as thin films or KBr discs using a Perkin-Elmer PARAGON 1000 FT-IR spectrometer, with selected peaks reported in cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer. Chemical shifts are reported in parts per million (ppm) and are referenced to the residual solvent peak, with coupling constants (*J*) measured in Hertz. Low resolution mass spectra (*m*/*z*) were recorded on either a Finnigan MAT 8340 instrument or a Finnigan MAT 900 XLT instrument. Major peaks are listed with intensities quoted as percentages of the base peak. Accurate mass measurements were recorded on a Finnigan MAT 900 XLT instrument. Optical rotations were recorded on an Optical Activity Ltd AA-10 automatic polarimeter, using a path length of 10 cm, in spectroscopic grade solvents (Aldrich), with concentrations (*c*) given in g per 100 cm^3, solvent and temperature as recorded. Melting points were recorded on a Büchi 535 melting point apparatus and are uncorrected. Elemental analyses were performed using an Exeter Analytical Inc CE-440 Elemental analyser. Single crystal X-ray diffraction data were collected on a Nonius Kappa CCD machine. Structural determination and refinement were achieved using the SHELZ suite of programmes; drawings were produced using ORTEX.

General procedure A: preparation of *N*-acyl-oxazolidin-2-ones

A solution of *n*-butyllithium in hexanes (1.1 eq.) was added dropwise *via* syringe to a stirred solution of oxazolidin-2-one

1 (1 eq.) in THF at −78 °C under a nitrogen atmosphere and the mixture was allowed to stir for 15 minutes. The appropriate acid chloride (1.1 eq.) was then added at −78 °C. The reaction was stirred at this temperature for 2 hours and allowed to warm to room temperature over a 1 hour period. Saturated $NH_4Cl_{(aq)}$ was added and the reaction extracted with CH_2Cl_2 (× 3). The combined organic extracts were washed with $NaHCO_{3(aq)}$, dried ($MgSO_4$), and concentrated *in vacuo* to afford the desired *N*-acyl oxazolidin-2-one.

General procedure B: preparation of *N*-acyl-oxazolidin-2-one-*syn*-aldols

A 0.5 M solution of 9-BBN-OTf in hexanes (1.2 eq.) was added *via* syringe to a stirred solution of *N*-acyloxazolidin-2-one (1 eq.) in CH_2Cl_2 at 0 °C and allowed to stir at this temperature for 5 minutes. *N*,*N*-diisopropylethylamine (1.4 eq.) was added, the reaction was stirred for 25 minutes at 0 °C before cooling to −78 °C. An aldehyde (1.1 eq.) was then added, the reaction was stirred for 2 hours and allowed to warm to 0 °C for 30 minutes. pH 7.0 phosphate buffer was added, allowed to stir for 5 min and a 2 : 1 solution of methanol–hydrogen peroxide added dropwise. The reaction was extracted with CH_2Cl_2 (× 3) and the combined organic extracts were washed with $NaHCO_{3(aq)}$, brine, dried ($MgSO_4$) and concentrated *in vacuo* to afford the desired *syn*-aldol.

General procedure C: preparation of trisubstituted (*E*)-α,β-unsaturated amides

A 0.5 M solution of KHMDS in toluene (1.5 eq.) was added dropwise to a stirred solution of *syn*-aldol (1 eq.) in THF at −78 °C under nitrogen, and the reaction was stirred at −78 °C for two hours. Saturated $NH_4Cl_{(aq)}$ was added and the reaction was extracted with CH_2Cl_2 (× 3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford the desired (*E*)-α,β-unsaturated amide.

General procedure D: preparation of 1,3-oxazinane-2,4-diones

A 1.0 M solution of Et_2Zn in toluene (0.1 eq.) was added dropwise to a stirred solution of *syn*-aldol (1 eq.) in CH_2Cl_2 at room temperature, and the reaction was stirred for 2 hours. Saturated $NH_4Cl_{(aq)}$ was added and the reaction was extracted with CH_2Cl_2 (× 3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford the desired *syn*-1,3-oxazinane-2,4-dione.

General procedure E: preparation of trisubstituted (*E*)-α,β-unsaturated acids

An (*E*)-α,β-unsaturated amide was refluxed in 6.0 M HCl for five hours. The reaction mixture was allowed to cool to room temperature, saturated with sodium chloride, and extracted with ethyl acetate (5 × 10 ml). The combined organic layers were dried over magnesium sulfate and the solvent was removed *in vacuo* to afford the desired (*E*)-α,β-unsaturated carboxylic acid.

General procedure F: preparation of trisubstituted (*E*)-α,β-oxazolines

Thionyl chloride (5 eq.) was added dropwise to a stirred solution of α,β-unsaturated amide (1 eq.) in CH_2Cl_2 in an ice bath, and the reaction mixture was stirred for 2 hours at this temperature. A 5.0 M solution of NaOH (3 mL) was added dropwise and the reaction was extracted with CH_2Cl_2 (× 3). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford the desired (*E*)-α,β-unsaturated oxazoline.

3-Propionyl-1,3-oxazolidin-2-one 2a[33]. Reaction of oxazolidin-2-one **1** (5.0 g, 57.47 mmol) with a 2.5 M solution of *n*-butyllithium in hexanes (25.30 mL, 63.2 mmol) and propionyl chloride (5.16 g, 63.2 mmol) in THF (250 mL), according to general procedure A, afforded after recrystallisation from hot ethyl acetate the title compound **2a** (5.940 g, 41.54 mmol) in 72% yield as a white crystalline solid, mp 77–79 °C (lit,[33] 80–81 °C); ν_{max} (KBr disc)/cm^{-1} 1773 (C=O)$_{ox}$, 1700 (C=O); δ_H(300 MHz, $CDCl_3$) 1.17 (3H, t, *J* 7.5, CH_2CH_3), 2.94 (2H, q, *J* 7.5, CH_2CH_3), 4.02 (2H, app t, *J* 8.0, CH_2N), 4.42 (2H, app t, *J* 8.0, CH_2O); δ_C($CDCl_3$) 8.7, 29.1, 42.9, 62.4, 154.0, 174.6; *m*/*z* (EI$^{+\bullet}$) 143 (49, M$^{+\bullet}$), 57 (100%, $CH_3CH_2CO^+$); HRMS (FAB$^+$) $C_6H_9NO_3$ [MH$^+$] requires 143.0577; found 143.0574.

3-(3-Methylbutanoyl)-1,3-oxazolidin-2-one 2b[41]. Reaction of oxazolidin-2-one **1** (9.905 g, 113.85 mmol) with a 2.5 M solution of *n*-butyllithium in hexanes (50.10 mL, 125.23 mmol) and iso-valeryl chloride (21.50 mL, 125.23 mmol) in THF (500 mL), according to general procedure A, afforded after purification through silica gel chromatography (40% ethyl acetate–petrol) the title compound **2b** (14.408 g, 84.26 mmol) in 74% yield as a colourless oil, ν_{max} (neat)/cm^{-1} 1779 (C=O)$_{ox}$, 1699 (C=O); δ_H(300 MHz, $CDCl_3$) 0.99 (6H, d, *J* 7.0, $CH(CH_3)_2$), 2.18 (1H, m, *J* 7.0, $CH(CH_3)_2$), 2.81 (2H, d, *J* 7.0, $CH_2{}^iPr$), 4.03 (2H, app t, *J* 8.0, CH_2N), 4.42 (2H, app t, *J* 8.0, CH_2O); δ_C($CDCl_3$) 22.8, 25.3, 42.9, 43.9, 62.3, 153.9, 173.2; *m*/*z* (CI$^+$, iso-butane) 172 (85, MH$^+$), 129 (82, MH$^+$–$CH(CH_3)_2$), 85 (100%); HRMS (FAB$^+$) $C_8H_{14}NO_3$ [MH$^+$] requires 172.0974; found 172.0974.

3-(3-Phenylpropanoyl)-1,3-oxazolidin-2-one 2c[42]. Reaction of oxazolidin-2-one **1** (1.496 g, 17.20 mmol) with a 2.5 M solution of *n*-butyllithium in hexanes (7.60 mL, 18.91 mmol) and phenylpropionyl chloride (2.80 mL, 18.91 mmol) in THF (90 mL), according to general procedure A, afforded after purification through silica gel chromatography (20% ethyl acetate–petrol) the title compound **2c** (2.765 g, 12.63 mmol) in 73% yield as a white solid, mp 100–101 °C; ν_{max} (KBr disc)/cm^{-1} 3008 (C–H)$_{ar}$, 1765 (C=O)$_{ox}$, 1692 (C=O); δ_H(300 MHz, $CDCl_3$) 2.91 (2H, t, *J* 7.5, CH_2CH_2Ph), 3.17 (2H, t, *J* 7.5, CH_2CH_2Ph), 3.90 (2H, app t, *J* 8.0, CH_2N), 4.29 (2H, app t, *J* 8.0, CH_2O), 7.09–7.24 (5H, m, Ar–*H*); δ_C($CDCl_3$) 30.6, 37.2, 42.9, 62.5, 126.6, 128.8, 128.9, 140.9, 153.9, 172.9; *m*/*z* (EI$^{+\bullet}$) 219 (55, M$^{+\bullet}$), 132 (27, $PhCH_2CH_2CO^+$), 104 (100), 88 (87, M$^{+\bullet}$–$PhCH_2CH_2CO^\bullet$); HRMS (ES$^+$) $C_{12}H_{17}N_2O_3$ [MNH_4^+] requires 237.1234; found 237.1237.

3-(2-Phenylacetyl)-1,3-oxazolidin-2-one 2d[43]. Reaction of oxazolidin-2-one **1** (9.90 g, 113.79 mmol) with a 1.6 M solution of *n*-butyllithium in hexanes (78.20 mL, 125.17 mmol) and phenyl acetyl chloride (21.50 mL, 125.17 mmol) in THF (500 mL), according to general procedure A, afforded after purification through silica gel chromatography (20% ethyl acetate–petrol) the title compound **2d** (14.404 g, 70.26 mmol) in 62% yield as a white solid, mp 61–63 °C (lit,[43] 64–65 °C); ν_{max} (KBr disc)/cm^{-1} 3010 (C–H)$_{ar}$, 1773 (C=O)$_{ox}$, 1696 (C=O); δ_H(300 MHz, $CDCl_3$) 3.92 (2H, app t, *J* 8.0, CH_2N), 4.25 (2H, s, CH_2Ph), 4.29 (2H, app t, *J* 8.0, CH_2O), 7.26–7.31 (5H, m, Ar–*H*); δ_C($CDCl_3$) 43.2, 47.8, 63.2, 128.1, 129.4, 130.0, 131.6, 154.7, 172.3; *m*/*z* (EI$^{+\bullet}$) 205 (30, M$^{+\bullet}$), 118 (100), 91 (60%, $PhCH_2^+$); HRMS (ES$^+$) $C_{11}H_{11}NO_3$ [MH$^+$] requires 205.0739; found 205.0742.

***syn*-3-{2-[Cyclohexyl(hydroxy)methyl]-3-methylbutanoyl}-1,3-oxazolidin-2-one 3a.** Reaction of 3-(3-methylbutanoyl)-1,3-oxazolidin-2-one **2b** (1.500 g, 8.77 mmol) with a 0.5 M solution of 9-BBN-OTf in hexanes (21.11 mL, 10.53 mmol), *N*,*N*-diisopropylethylamine (1.99 mL, 11.40 mmol) and cyclocarboxaldehyde (1.17 mL, 9.65 mmol) in CH_2Cl_2 (40 mL), according to general procedure B, afforded after purification through silica gel chromatography (gradient, 10–20% ethyl acetate–petrol) the title compound *syn*-**3a** (1.451 g, 5.11 mmol) in 58% yield as a white solid, mp 131–133 °C; ν_{max} (KBr disc)/cm^{-1} 3510 (s, OH), 1773 (C=O)$_{ox}$, 1676 (C=O); δ_H(300 MHz, $CDCl_3$) 1.02 (3H, d, *J* 7.0, $CH(CH_3)_2$), 1.03 (3H, d, *J* 7.0, $CH(CH_3)_2$), 1.12–1.27 (4H, m, Cy–*H*), 1.61–1.67

(2H, m, Cy–*H*), 1.73–1.77 (2H, m, Cy–*H*), 1.83–1.91 (2H, m, Cy–*H*), 2.04–2.10 (1H, m, Cy–*H*), 2.31 (1H, m, *J* 7.0, 5.0, C*H*$(CH_3)_2$), 3.72–3.78 (1H, m, C*H*OH), 4.04 (2H, app t, *J* 8.0, CH_2N), 4.22 (1H, dd, *J* 7.0, 5.0, C*H*^{i}Pr), 4.41 (2H, app t, *J* 8.0, CH_2O); δ_C($CDCl_3$) 19.6, 21.5, 26.7, 27.4, 28.2, 30.6, 41.7, 43.0, 49.3, 61.9, 76.0, 153.7, 175.6; *m*/*z* (FAB^+) 284 (97, MH^+), 266 (100%, M^+–OH); HRMS (FAB^+) $C_{15}H_{26}NO_4$ [MH^+] requires 284.1862; found 284.1868.

***syn*-3-(3-Hydroxy-2-methyl-3-phenylpropanoyl)-1,3-oxazolidin-2-one 3b[27].** Reaction of 3-propionyl-1,3-oxazolidin-2-one **2a** (0.545 g, 3.81 mmol) with a 0.5 M solution of 9-BBN-OTf in hexanes (9.14 mL, 4.57 mmol), *N*,*N*-diisopropylethylamine (0.86 mL, 4.95 mmol) and benzaldehyde (0.43 mL, 4.19 mmol) in CH_2Cl_2 (20 mL), according to general procedure B, afforded after purification through silica gel chromatography (gradient, 20–30% ethyl acetate–petrol) the title compound *syn*-**3b** (0.653 g, 2.62 mmol) in 69% yield as a white crystalline solid, mp 102–104 °C (lit,[27] 105–106 °C); ν_{max} (KBr disc)/cm^{-1} 3561 (s, OH), 1766 $(C{=}O)_{ox}$, 1682 (C=O); δ_H(300 MHz, $CDCl_3$) 1.15 (3H, d, *J* 7.0, CH_3), 3.07 (1H, d, *J* 3.0, O*H*), 3.95–4.07 (2H, m, CH_2N), 4.12 (1H, qd, *J* 7.0, 3.0, CHCH_3), 4.31–4.45 (2H, m, CH_2O), 5.13 (1H, app t, *J* 3.0, C*H*OH), 7.24–7.43 (5H, m, Ar–*H*); δ_C($CDCl_3$) 10.8, 43.0, 44.6, 62.4, 73.9, 126.4, 127.9, 128.6, 141.6, 153.5, 177.2; *m*/*z* (CI^+, NH_3) 267 (41, MNH_4^+), 250 (10, MH^+), 232 (38, M^+–OH), 206 (22, MH^+–CO_2), 161 (100%); HRMS (FAB^+) $C_{13}H_{16}NO_4$ [MH^+] requires 250.1079; found 250.1081.

***syn*-3-(3-Hydroxy-2-methylpentanoyl)-1,3-oxazolidin-2-one 3c.** Reaction of 3-propionyl-1,3-oxazolidin-2-one **2a** (0.991 g, 6.93 mmol) with a 1.0 M solution of 9-BBN-OTf in CH_2Cl_2 (8.39 mL, 8.39 mmol), *N*,*N*-diisopropylethylamine (1.70 mL, 9.79 mmol) and propionaldehyde (0.56 mL, 7.69 mmol) in CH_2Cl_2 (35 mL), according to general procedure B, afforded after purification through silica gel chromatography (gradient, 25–40% ethyl acetate–petrol) the title compound *syn*-**3c** (0.427 g, 2.12 mmol) in 31% yield as a white solid, mp 60–62 °C; $C_9H_{15}NO_4$ requires C, 53.7; H, 7.51; N, 6.96%; found C, 53.6; H, 7.45; N, 6.89%; ν_{max}(KBr disc)/cm^{-1} 3471 (br, OH), 1752 $(C{=}O)_{ox}$, 1696 (C=O); δ_H(300 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.5, CH_2CH_3), 1.13 (3H, d, *J* 7.0, C*H*CH_3), 1.44 (2H, m, CH_2CH_3), 2.78 (1H, br s, O*H*), 3.79–3.89 (2H, m, C*H*OH, C*H*CH_3), 4.01–4.07 (2H, m, CH_2N), 4.37 (2H, app t, *J* 8.5, CH_2O); δ_C($CDCl_3$) 8.3, 8.5, 24.8, 39.6, 40.8, 60.1, 71.2, 151.4, 175.6; *m*/*z* (CI^+, iso-butane) 202 (100, MH^+), 184 (95, M^+–OH), 143 (57%, M^+–CH_3CH_2CHOH); HRMS (FAB^+) $C_9H_{16}NO_4$ [MH^+] requires 202.1079; found 202.1080.

***syn*-3-(2-Benzyl-3-hydroxydecanoyl)-1,3-oxazolidin-2-one 3d.** Reaction of 3-(3-phenylpropanoyl)-1,3-oxazolidin-2-one **2c** (0.500 g, 2.28 mmol) with a 0.5 M solution of 9-BBN-OTf in hexanes (5.48 mL, 2.74 mmol), *N*,*N*-diisopropylethylamine (0.56 mL, 3.20 mmol) and octanal (0.39 mL, 2.51 mmol) in CH_2Cl_2 (10 mL), according to general procedure B, afforded after purification through silica gel chromatography (20% ethyl acetate–petrol) the title compound *syn*-**3d** (0.582 g, 1.68 mmol) in 74% yield as a colourless oil, ν_{max}(neat)/cm^{-1} 3474 (br, OH), 1775 $(C{=}O)_{ox}$, 1695 (C=O); δ_H(300 MHz, $CDCl_3$) 0.81 (3H, t, *J* 7.0, CH_3), 1.16–1.28 (8H, m, CH_2), 1.44–1.52 (4H, m, CH_2), 2.65 (1H, br s, O*H*), 2.92 (1H, dd, *J* 13.0, 5.5, C$H_A$$H_B$Ph), 2.99 (1H, dd, *J* 13.0, 10.0, C$H_A$$H_B$Ph), 3.62 (1H, ddd, *J* 10.0, 9.0, 6.0, C$H_A$$H_B$N), 3.73–4.00 (3H, m, C$H_A$$H_B$N, C*H*OH, C$H_A$$H_B$O), 4.18 (1H, app dt, *J* 9.0, 6.0, C$H_A$$H_B$O), 4.33–4.40 (1H, m, C*H*CH_2Ph), 7.11–7.19 (5H, m, Ar–*H*); δ_C($CDCl_3$) 14.5, 23.0, 26.4, 29.6, 29.9, 32.2, 33.5, 34.4, 42.9, 49.5, 62.1, 72.6, 126.8, 128.7, 129.4, 139.3, 153.7, 175.9; *m*/*z* (CI^+, NH_3) 365 (11, MNH_4^+), 348 (13, MH^+), 237.2 (100%); HRMS (ES^+) $C_{20}H_{30}NO_4$ [MH^+] requires 348.2169; found 348.2171.

***syn*-3-(3-Hydroxy-2-isopropylpentanoyl)-1,3-oxazolidin-2-one 3e[41].** Reaction of 3-(3-methylbutanoyl)-1,3-oxazolidin-2-one **2b** (0.965 mg, 5.85 mmol) with a 0.5 M solution of 9-BBN-OTf in CH_2Cl_2 (14.0 mL, 7.02 mmol), *N*,*N*-diisopropylethylamine (1.43 mL, 8.19 mmol) and propionaldehyde (0.47 mL, 6.44 mmol) in CH_2Cl_2 (30 mL), according to general procedure B, afforded after purification through silica gel chromatography (gradient, 25–40% ethyl acetate–petrol) the title compound *syn*-**3e** (0.644 g, 2.81 mmol) in 48% yield as a white solid, mp 60–62 °C; ν_{max}(KBr disc)/cm^{-1} 3463 (br, OH), 1752 $(C{=}O)_{ox}$, 1696 (C=O); δ_H(300 MHz, $CDCl_3$) 0.85 (3H, d, *J* 7.0, CH(CH_3)$_2$), 0.90 (3H, d, *J* 7.0, CH(CH_3)$_2$), 0.91 (3H, t, *J* 7.0, CH_2CH_3), 1.35 (1H, ddq, *J* 14.0, 10.0, 7.0, C$H_A$$H_B$$CH_3$), 1.51 (1H, dqd, *J* 14.0, 7.0, 2.3, C$H_A$$H_B$$CH_3$), 2.12 (1H, m, *J* 8.0, 7.0, C*H*$(CH_3)_2$), 2.54 (1H, br s, OH), 3.83 (1H, app t, *J* 7.0, C*H*^{i}Pr), 3.91–4.02 (3H, m, CH_2N, C*H*OH), 4.30–4.37 (2H, m, CH_2O); δ_C($CDCl_3$) 9.7, 19.2, 19.9, 24.4, 27.0, 41.8, 53.1, 60.8, 72.1, 153.3, 173.6; *m*/*z* (CI^+, iso-butane) 230 (5, MH^+), 212 (8, M^+–OH), 171 (34%, M^+–CH_3CH_2CHOH); HRMS (FAB^+) $C_{11}H_{20}NO_4$ [MH^+] requires 230.1392; found 230.1394.

***syn*-3-{2-[Hydroxy(phenyl)methyl]-3-methylbutanoyl}-1,3-oxazolidin-2-one 3f.** Reaction of 3-(3-methylbutanoyl)-1,3-oxazolidin-2-one **2b** (0.993 g, 5.81 mmol) with a 0.5 M solution of 9-BBN-OTf in hexanes (11.7 mL, 5.85 mmol), *N*,*N*-diisopropylethylamine (1.40 mL, 8.19 mmol) and benzaldehyde (0.65 mL, 6.43 mmol) in CH_2Cl_2 (30 mL), according to general procedure B, afforded after purification through silica gel chromatography (25% ethyl acetate–petrol) the title compound *syn*-**3f** (0.811 g, 2.93 mmol) in 50% yield as a white solid, mp 93–95 °C; ν_{max}(KBr disc)/cm^{-1} 3450 (s, OH), 1751 $(C{=}O)_{ox}$, 1695 (C=O); δ_H(300 MHz, $CDCl_3$) 1.01 (3H, d, *J* 7.0, CH(CH_3)$_2$), 1.08 (3H, d, *J* 7.0, CH(CH_3)$_2$), 2.36 (1H, m, *J* 7.0, 5.5, C*H*$(CH_3)_2$), 2.41 (1H, d, *J* 3.0, O*H*), 3.62 (1H, ddd, *J* 11.0, 9.5, 7.0, C$H_A$$H_B$N), 3.84 (1H, ddd, *J* 11.0, 9.5, 7.0, C$H_A$$H_B$N), 4.07 (1H, app dt, *J* 9.0, 8.0, C$H_A$$H_B$O), 4.24 (1H, app dt, *J* 9.0, 8.0, C$H_A$$H_B$O), 4.48 (1H, dd, *J* 8.0, 5.5, C*H*^{i}Pr), 5.01 (1H, dd, *J* 8.0, 3.0, C*H*OH), 7.25–7.40 (5H, m, Ar–*H*); δ_C($CDCl_3$) 18.0, 19.8, 27.1, 41.3, 53.0, 60.3, 72.9, 125.6, 126.7, 127.1, 140.9, 152.0, 172.7; *m*/*z* (CI^+, NH_3) 295 (8, MNH_4^+), 278 (5, MH^+), 260 (28, M^+–OH), 234 (9, M^+-^{i}Pr), 105 (100%); HRMS (ES^+) $C_{15}H_{23}N_2O_4$ [MNH_4^+] requires 295.1652; found 295.1653.

***syn*-3-{2-[Hydroxy(4-methoxyphenyl)methyl]-3-methylbutanoyl}-1,3-oxazolidin-2-one 3g.** Reaction of 3-(3-methylbutanoyl)-1,3-oxazolidin-2-one **2b** (1.500 g, 8.77 mmol) with a 0.5 M solution of 9-BBN-OTf in hexanes (21.10 mL, 10.53 mmol), *N*,*N*-diisopropylethylamine (1.99 mL, 11.40 mmol) and *p*-anisaldehyde (1.17 mL, 9.65 mmol) in CH_2Cl_2 (40 mL), according to general procedure B, afforded after purification through silica gel chromatography (gradient, 10–20% ethyl acetate–petrol) the title compound *syn*-**3g** (1.592 g, 5.18 mmol) in 60% yield as a white crystalline solid, mp 117–118 °C; ν_{max} (KBr disc)/cm^{-1} 3449 (s, OH), 1755 $(C{=}O)_{ox}$, 1691 (C=O); δ_H(300 MHz, $CDCl_3$) 1.02 (3H, d, *J* 7.0, CH(CH_3)$_2$), 1.08 (3H, d, *J* 7.0, CH(CH_3)$_2$), 2.24 (1H, d, *J* 3.5, O*H*), 2.35 (1H, m, *J* 7.0, 5.5, C*H*$(CH_3)_2$), 3.65 (1H, ddd, *J* 11.0, 9.5, 7.0, C$H_A$$H_B$N), 3.79 (3H, s, ArOC$H_3$), 3.86 (1H, ddd, *J* 11.0, 9.5, 7.0, C$H_A$$H_B$N), 4.12 (1H, app dt, *J* 9.0, 7.0, C$H_A$$H_B$O), 4.26 (1H, app td, *J* 9.0, 7.0, C$H_A$$H_B$O), 4.48 (1H, dd, *J* 8.0, 5.5, C*H*^{i}Pr), 4.97 (1H, dd, *J* 8.0, 3.5, C*H*OH), 6.84 (2H, d, *J* 8.5, Ar–*H*), 7.30 (2H, d, *J* 8.5, Ar–*H*); δ_C($CDCl_3$) 19.5, 21.3, 28.7, 42.9, 54.5, 55.6, 61.8, 74.0, 114.0, 128.5, 134.6, 153.6, 159.6, 174.2; *m*/*z* ($EI^{+\bullet}$) 307 (12, $M^{+\bullet}$), 171 (28, $M^{+\bullet}$–$ArCHOH^\bullet$), 149 (100%); HRMS (FAB^+) $C_{16}H_{21}NO_5$ [MH^+] requires 307.1420; found 307.1426.

***syn*-3-(3-Hydroxy-2-phenylpentanoyl)-1,3-oxazolidin-2-one 3h.** Reaction of 3-(2-phenylacetyl)-1,3-oxazolidin-2-one **2d** (0.994 g, 4.85 mmol) with a 1.0 M solution of 9-BBN-OTf in CH_2Cl_2 (5.86 mL, 5.86 mmol), *N*,*N*-diisopropylethylamine (1.20 mL, 6.83 mmol) and propionaldehyde (0.39 mL, 5.37 mmol) in CH_2Cl_2 (20 mL), according to general procedure B, afforded after purification through silica gel chromatography

(25% ethyl acetate–petrol) the title compound *syn*-**3h** (0.464 g, 1.76 mmol) in 37% yield as a colourless oil, ν_{max}(neat)/cm^{-1} 3519 (br, OH), 1771 (C=O)$_{ox}$, 1694 (C=O); δ_H(300 MHz, $CDCl_3$) 0.99 (3H, t, *J* 7.5, CH_2CH_3), 1.35–1.48 (2H, m, CH_2CH_3), 2.70 (1H, d, *J* 3.0, O*H*), 3.92 (1H, ddd, *J* 11.0, 9.5, 6.5, CH_AH_BN), 4.06 (1H, ddd, *J* 11.0, 9.5, 7.0, CH_AH_BN), 4.11–4.17 (1H, m, C*H*OH), 4.29 (1H, app dt, *J* 9.5, 8.0, CH_AH_BO), 4.38 (1H, app dt, *J* 9.5, 8.0, CH_AH_BO), 5.04 (1H, d, *J* 5.5, C*H*Ph), 7.26–7.44 (5H, m, Ar–H); δ_C($CDCl_3$) 10.5, 27.6, 42.9, 53.5, 62.0, 74.0, 128.1, 128.7, 130.3, 134.2, 153.0, 174.2; *m*/*z* (CI$^+$, NH_3) 281 (20, MNH_4^+), 264 (19, MH$^+$), 223 (100%); HRMS (ES$^+$) $C_{14}H_{18}NO_4$ [MH$^+$] requires 264.1230, found 264.1227.

***syn*-3-[(*E*)-3-Hydroxy-2-isopropyl-4-hexenoyl]-1,3-oxazolidin-2-one 3i.** Reaction of 3-(3-methylbutanoyl)-1,3-oxazolidin-2-one **2b** (0.965 g, 5.85 mmol) with a 0.5 M solution of 9-BBN-OTf in hexanes (14.10 mL, 7.02 mmol), *N*,*N*-diisopropylethylamine (1.32 mL, 7.60 mmol) and *trans*-crotonaldehyde (0.53 mL, 6.44 mmol) in CH_2Cl_2 (30 mL), according to general procedure B, afforded after purification through silica gel chromatography (25% ethyl acetate–petrol) the title compound *syn*-**3i** (1.090 g, 4.54 mmol) in 72% yield as a low-melting point white solid, ν_{max}(nujol)/cm^{-1} 3454 (br, OH), 1770 (C=O)$_{ox}$, 1690 (C=O); δ_H(300 MHz, $CDCl_3$) 0.92 (3H, d, *J* 6.5, $CH(CH_3)_2$), 0.97 (3H, d, *J* 6.5, $CH(CH_3)_2$), 1.72 (3H, d, *J* 5.5, $CH{=}CHCH_3$), 1.99–2.11 (1H, m, $CH(CH_3)_2$), 2.23 (1H, br s, O*H*), 4.01–4.10 (3H, m, CH_2N, C*H*^{i}Pr), 4.34–4.48 (3H, m, CH_2O, C*H*OH), 5.60–5.81 (2H, m, $CH{=}CHCH_3$); δ_C($CDCl_3$) 18.2, 20.4, 21.1, 28.6, 43.2, 54.3, 62.0, 73.5, 130.0, 130.5, 154.7, 174.7; *m*/*z* (CI$^+$, iso-butane) 242 (6, MH$^+$), 224.1 (75, M$^+$–OH), 171.0 (64, M$^+$–CHOHCHCHCH$_3$), 156.0 (100%); HRMS (FAB$^+$) $C_{12}H_{20}NO_4$ [MH$^+$] requires 242.1392; found 242.1393.

***syn*-3-[(*E*)-3-Hydroxy-2-methyl-5-phenyl-4-pentenoyl]-1,3-oxazolidin-2-one 3j.** Reaction of 3-propionyl-1,3-oxazolidin-2-one **2a** (0.500 g, 3.50 mmol) with a 0.5 M solution of 9-BBN-OTf in hexanes (8.40 mL, 4.20 mmol), *N*,*N*-diisopropylethylamine (0.79 mL, 4.55 mmol) and *trans*-cinnamaldehyde (0.49 mL, 3.85 mmol) in CH_2Cl_2 (15 mL), according to general procedure B, afforded after purification through silica gel chromatography (gradient, 20–40% EtOAc–petrol) the title compound *syn*-**3j** (0.841 g, 3.06 mmol) in 88% yield as a white crystalline solid, mp 100–101 °C; ν_{max}(KBr disc)/cm^{-1} 3476 (s, OH), 1762 (C=O)$_{ox}$, 1683 (C=O); δ_H(300 MHz, $CDCl_3$) 1.17 (3H, d, *J* 7.0, CH_3), 2.97 (1H, d, *J* 1.0, O*H*), 3.88–3.99 (3H, m, CH_2N, C*H*CH$_3$), 4.28–4.34 (2H, m, CH_2O), 4.58 (1H, ddd, *J* 6.0, 4.0, 1.0, C*H*OH), 6.14 (1H, dd, *J* 16.0, 6.0, *H*C=CHPh), 6.59 (1H, d, *J* 16.0, HC=C*H*Ph), 7.15–7.34 (5H, m, Ar–*H*); δ_C($CDCl_3$) 11.6, 43.0, 43.5, 62.4, 73.2, 126.9, 128.1, 129.0 (2C), 131.8, 136.9, 153.8, 176.8; *m*/*z* (EI$^{+\bullet}$) 275 (7, M$^{+\bullet}$), 143 (42, M$^{+\bullet}$–PhCHCHCHOH$^\bullet$), 104.1 (100%); HRMS (ES$^+$) $C_{15}H_{21}N_2O_4$ [MNH_4^+] requires 293.1496; found 293.1495.

(*E*)-3-Cyclohexyl-*N*-(2-hydroxyethyl)-2-isopropyl-2-propenamide 4a. Reaction of *syn*-3-{2-[cyclohexyl(hydroxy)methyl]-3-methylbutanoyl}-1,3-oxazolidin-2-one **3a** (0.100 g, 0.35 mmol) with a 0.5 M solution of KHMDS in toluene (1.06 mL, 0.53 mmol) in THF (2 mL), according to general procedure C, gave the title compound (*E*)-**4a** (0.075 g, 0.31 mmol) in 94% de. The crude product was purified for analysis by silica gel chromatography (gradient, 20–30% ethyl acetate–petrol), to afford the title compound (*E*)-**4a** (0.064 g, 0.27 mmol) in 77% yield and >95% de as a white solid, mp 84–86 °C; ν_{max}(KBr disc)/cm^{-1} 3291 (br, OH, NH), 1652 (C=O), 1619 (C=C), 1541 (C=O); δ_H(300 MHz, $CDCl_3$) 1.01–1.37 (6H, m, Cy-*H*), 1.18 (6H, d, *J* 7.0, $CH(CH_3)_2$), 1.60–1.78 (4H, m, Cy-*H*), 2.25–2.39 (1H, m, Cy-*H*), 2.83 (1H, m, *J* 7.0, $CH(CH_3)_2$), 2.95 (1H, t, *J* 4.5, O*H*), 3.44 (2H, app q, *J* 5.5, 4.5, CH_2NH), 3.74 (2H, app q, *J* 5.5, 4.5, CH_2OH), 5.59 (1H, d, *J* 10.0, C=C*H*), 6.08 (1H, br s, N*H*); δ_C($CDCl_3$) 22.1, 26.1, 26.2, 28.6, 33.3, 37.0, 42.9, 63.3, 137.9, 142.0, 173.1; *m*/*z* (EI$^{+\bullet}$) 239 (65, M$^{+\bullet}$), 224 (85, M$^{+\bullet}$–$CH_3^\bullet$), 179 (68%, M$^{+\bullet}$–$HOCH_2CH_2NH^\bullet$); HRMS (FAB$^+$) $C_{14}H_{25}NO_2$ [MH$^+$] requires 239.1885; found 239.1886.

X-Ray crystal data for 4a

($C_{14}H_{25}NO_2$): M_r = 239.35, *T* = 150(2) K, monoclinic, space group $P2_1/c$, *a* = 17.3540(2), *b* = 9.79700(10), *c* = 17.7370(2) Å, β = 104.153(1)°, *V* = 2924.06(7) Å^3, *Z* = 8, ρ_{calcd} = 1.087 Mg m^{-3}, μ = 0.071 mm^{-1}, λ = 0.71073 Å, θ_{max} = 27.46°, 43295 measured reflections, 6676 independent reflections [*R*(int) = 0.0787], GOF on F^2 = 1.007, R_1 = 0.0453, wR_2 = 0.1035 ($I>2\sigma(I)$), R_1 = 0.0818, wR_2 = 0.1198 (for all data), largest difference peak and hole 0.232 and −0.215 e Å^{-3}. Crystal data were collected on a Nonius Kappa CCD diffractometer. The structure was solved by direct methods and refined on all F^2 data using the SHELX-97 suite of programs.[44] The asymmetric unit was seen to consist of two molecules, one of which exhibited 55 : 45 positional disorder in the cyclohexyl carbons. All hydrogen atoms were included at calculated positions, with the exception of the H1 and H1A (hydroxyl groups), which were located and refined. The supramolecular array is dominated by extensive hydrogen-bonding.†

(*E*)-*N*-(2-Hydroxyethyl)-2-methyl-3-phenyl-2-propenamide 4b. Reaction of *syn*-3-(3-hydroxy-2-methyl-3-phenylpropanoyl)-1,3-oxazolidin-2-one **3b** (0.200 g, 0.80 mmol) with a 0.5 M solution of KHMDS in toluene (2.41 mL, 1.20 mmol) in THF (4 mL), according to general procedure C, afforded the title compound (*E*)-**4b** (0.143 g, 0.70 mmol) in 91% yield and >95% de as a white solid, mp 101–103 °C; ν_{max} (KBr disc)/cm^{-1} 3284 (br, OH, NH), 1644 (C=O), 1620 (C=C), 1575 (C=O); δ_H(300 MHz, $CDCl_3$) 2.04 (3H, d, *J* 1.0, C=C(CH_3)), 3.08 (1H, br s, O*H*), 3.46–3.51 (2H, m, CH_2N), 3.74 (2H, app t, *J* 5.0, CH_2O), 6.48 (1H, br s, N*H*), 7.19 (1H, s, C=C*H*), 7.20–7.33 (5H, m, Ar–H); δ_C($CDCl_3$) 14.6, 43.3, 62.8, 128.3, 128.7, 129.7, 131.7, 135.0, 136.3, 171.2; *m*/*z* (CI$^+$, NH_3) 206 (100%, MH$^+$); HRMS (FAB$^+$) $C_{12}H_{16}NO_2$ [MH$^+$] requires 206.1176, found 206.1177.

(*E*)-*N*-(2-Hydroxyethyl)-2-methyl-2-pentenamide 4c. Reaction of *syn*-3-(3-hydroxy-2-methylpentanoyl)-1,3-oxazolidin-2-one **3c** (0.050 g, 0.25 mmol) with a 0.5 M solution of KHMDS in toluene (0.75 mL, 0.37 mmol) in THF (3 mL), according to general procedure C, afforded the title compound (*E*)-**4c** (0.026 g, 0.17 mmol) in 67% yield and >95% de as a white solid of low melting point (<30 °C), ν_{max}(KBr disc)/cm^{-1} 3405 (br, OH, NH), 1701 (C=O), 1615 (C=C), 1538 (C=O); δ_H(300 MHz, $CDCl_3$) 1.04 (3H, t, *J* 7.5, CH_2CH_3), 1.85 (3H, s, CH_3), 2.17 (2H, app pentet, *J* 7.5, CH_2CH_3), 2.86 (1H, br s, O*H*), 3.50 (2H, app q, *J* 6.0, 5.0, CH_2NH), 3.77 (2H, app t, *J* 6.0, CH_2OH), 6.19 (1H, s, N*H*), 6.38 (1H, t, *J* 7.5, C=C*H*); δ_C($CDCl_3$) 11.5, 12.2, 20.6, 41.7, 61.4, 128.7, 137.5, 169.7; *m*/*z* (CI$^+$, NH_3) 158 (100%, MH$^+$); HRMS (ES$^+$) $C_8H_{16}NO_2$ [MH$^+$] requires 158.1176; found 158.1179.

(*E*)-2-Benzyl-*N*-(2-hydroxyethyl)-2-decenamide 4d. Reaction of *syn*-3-(2-benzyl-3-hydroxydecanoyl)-1,3-oxazolidin-2-one **3d** (0.135 g, 0.39 mmol) with a 0.5 M solution of KHMDS in toluene (1.17 mL, 0.58 mmol) in THF (3 mL), according to general procedure C, gave the title compound (*E*)-**4d** (0.110 g, 0.36 mmol) in 92% de. The crude product was purified for analysis by silica gel chromatography (60% ethyl acetate–petrol) to afford the title compound (*E*)-**4d** (0.108 g, 0.36 mmol) in 91% yield and >95% de as a colourless oil, ν_{max}(neat)/cm^{-1} 3342 (br, OH, NH), 1656 (C=O), 1620 (C=C), 1537 (C=O); δ_H(300 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.0, CH_3), 1.23–1.28 (8H, m, Alk-*H*), 1.39–1.46 (2H, m, CH_2), 2.21 (2H, app q, *J* 7.5, $CH{=}CCH_2$), 2.97 (1H, br s, O*H*), 3.33 (2H, app q, *J* 5.5, 5.0, CH_2NH), 3.57 (2H, m, CH_2OH), 3.69 (2H, s, CH_2Ph), 6.17

† CCDC reference number 207151. See http://dx.doi.org/10.1039/b503633j for crystallographic data in CIF or other electronic format.

(1H, br t, *J* 5.0, N*H*), 6.54 (1H, t, *J* 7.5, C=C*H*), 7.16–7.30 (5H, m, Ar–*H*); δ_C($CDCl_3$) 14.5, 23.0, 28.9, 29.3, 29.5, 29.8, 32.1, 33.1, 43.1, 62.9, 126.8, 128.5, 129.1, 134.0, 139.0, 139.3, 170.5; *m*/*z* ($EI^{+\bullet}$) 303 (10, $M^{+\bullet}$), 243 (13, $M^{+\bullet}$–$HOCH_2CH_2NH^{\bullet}$), 91 (100%, $PhCH_2^+$); HRMS (ES^+) $C_{19}H_{30}NO_2$ [MH^+] requires 304.2271; found 304.2275.

(*E*)-*N*-(2-Hydroxyethyl)-2-isopropyl-2-pentenamide 4e[45]. Reaction of *syn*-3-(3-hydroxy-2-methylpentanoyl)-1,3-oxazolidin-2-one **3e** (0.100 g, 0.44 mmol) with a 0.5 M solution of KHMDS in toluene (1.30 mL, 0.65 mmol) in THF (3 mL), according to general procedure C, afforded the title compound (*E*)-**4e** (0.080 g, 0.43 mmol) in 99% yield and >95% de as a colourless oil, ν_{max}(neat)/cm^{-1} 3338 (br, OH, NH), 1653 (C=O), 1617 (C=C), 1534 (C=O); δ_H(300 MHz, $CDCl_3$) 1.03 (3H, t, *J* 7.5, CH_2CH_3), 1.16 (6H, d, *J* 7.0, $CH(CH_3)_2$), 2.14 (2H, app pentet, *J* 7.5, CH_2CH_3), 2.81 (1H, septet, *J* 7.0, $CH(CH_3)_2$), 3.43 (2H, app q, *J* 5.5, 4.5, CH_2NH), 3.50 (1H, br s, O*H*), 3.73 (2H, app t, *J* 5.0, CH_2OH), 5.77 (1H, t, *J* 7.5, C=C*H*), 6.26 (1H, br s, N*H*); δ_C($CDCl_3$) 13.2, 20.1, 20.7, 27.2, 41.7, 61.8, 133.0, 142.2, 171.9; *m*/*z* (CI^+, iso-butane) 186 (88, MH^+), 185 (32, M^+), 125 (100%, M^+–$HOCH_2CH_2NH$); HRMS (FAB^+) $C_{10}H_{20}NO_2$ [MH^+] requires 186.1494, found 186.1495.

(*E*)-*N*-(2-Hydroxyethyl)-2-isopropyl-3-phenyl-2-propenamide 4f. Reaction of *syn*-3-{2-[hydroxy(phenyl)methyl]-3-methylbutanoyl}-1,3-oxazolidin-2-one **3f** (0.085 g, 0.31 mmol) with a 0.5 M solution of KHMDS in toluene (1.08 mL, 0.54 mmol) in THF (3 mL), according to general procedure C, afforded title compound (*E*)-**4f** (0.068 g, 0.29 mmol) in 92% de. The crude product was purified for analysis by silica gel chromatography (40% ethyl acetate–petrol) to afford the title compound (*E*)-**4f** (0.065 g, 0.22 mmol) in 90% yield and >95% de as a white solid, mp 101–103 °C; ν_{max} (KBr disc)/cm^{-1} 3317 (s, OH, NH), 1641 (C=O), 1612 (C=C), 1538 (C=O); δ_H(300 MHz, $CDCl_3$) 1.24 (6H, d, *J* 7.0, $CH(CH_3)_2$), 2.95 (1H, br s, O*H*), 3.07 (1H, septet, *J* 7.0, $CH(CH_3)_2$), 3.52 (2H, app q, *J* 5.5, 5.0, CH_2NH), 3.79 (2H, app t, *J* 5.0, CH_2OH), 6.33 (1H, br s, N*H*), 6.79 (1H, br s, C=C*H*), 7.25–7.39 (5H, m, Ar–*H*); δ_C($CDCl_3$) 21.9, 28.5, 42.8, 63.0, 128.0, 128.8, 129.1, 130.1, 136.1, 145.7, 172.4; *m*/*z* ($EI^{+\bullet}$) 233 (19, $M^{+\bullet}$), 173 (48, $M^{+\bullet}$–$HOCH_2CH_2NH^{\bullet}$), 145(57, $M^{+\bullet}$–$HOCH_2CH_2NHCO^{\bullet}$), 91 (100%, $PhCH_2^+$); HRMS (ES^+) $C_{14}H_{20}NO_2$ [MH^+] requires 234.1489, found 234.1489.

(*E*)-*N*-(2-Hydroxyethyl)-2-isopropyl-3-(4-methoxyphenyl)-2-propenamide 4g. Reaction of *syn*-3-{2-[hydroxy(4-methoxyphenyl)methyl]-3-methylbutanoyl}-1,3-oxazolidin-2-one **3g** (0.200 g, 0.65 mmol) with a 1.0 M solution of KHMDS in toluene (1.95 mL, 0.98 mmol) in THF (4 mL), according to general procedure C, gave the title compound (*E*)-**4g** (0.155 g, 0.59 mmol) in 90% de. The crude product was purified for analysis by silica gel chromatography (40% ethyl acetate–petrol) to afford the title compound (*E*)-**4g** (0.149 g, 0.57 mmol) in 88% yield and >95% de as a white solid, mp 91–93 °C; ν_{max} (KBr disc)/cm^{-1} 3279 (s, OH), 3064 $(C=C)_{ar}$, 2834 $(C–H)_{OMe}$, 1645 (C=O), 1620 (C=C), 1606 $(C=C)_{ar}$, 1542 (C=O), 1510 $(C=C)_{ar}$; δ_H(300 MHz, $CDCl_3$) 1.24 (6H, d, *J* 7.0, $CH(CH_3)_2$), 3.09 (1H, septet, *J* 7.0, $CH(CH_3)_2$), 3.18 (1H, br s, O*H*), 3.50 (2H, app dt, *J* 5.5, 5.0, CH_2NH), 3.75–3.85 (2H, m, CH_2OH), 3.82 (3H, s, $ArOCH_3$), 6.38 (1H, br s, N*H*), 6.73 (1H, s, C=C*H*), 6.89 (2H, d, *J* 9.0, Ar–*H*), 7.21 (2H, d, *J* 9.0, Ar–*H*); δ_C($CDCl_3$) 21.9, 28.4, 42.8, 55.7, 62.9, 114.2, 128.5, 129.7, 130.5, 144.1, 159.4, 172.6; *m*/*z* ($EI^{+\bullet}$) 263 (35, $M^{+\bullet}$), 203 (26, $M^{+\bullet}$–$HOCH_2CH_2NH^{\bullet}$), 84 (100%); HRMS (FAB^+) $C_{15}H_{21}NO_3$ [MH^+] requires 263.1521; found 263.1518.

(*E*)-*N*-(2-Hydroxyethyl)-2-phenyl-2-pentenamide 4h. Reaction of *syn*-3-(3-hydroxy-2-phenylpentanoyl)-1,3-oxazolidin-2-one **3h** (0.200 g, 0.76 mmol) with a 0.5 M solution of KHMDS in toluene (2.24 mL, 1.12 mmol) in THF (2 mL), according to general procedure C, gave a mixture of the title compound (*E*)-**4h** (80%) in >95% de and the parent *N*-acyl oxazolidin-2-one **2d** (20%). The crude product was purified by silica gel chromatography (40% ethyl acetate–petrol) to afford the title compound (*E*)-**4h** (0.078 g, 0.35 mmol) in 47% yield and >95% de as a colourless oil, ν_{max} (neat)/cm^{-1} 3418 (br, OH, NH), 1657 (C=O), 1617 (C=C), 1522 (C=O); δ_H(300 MHz, $CDCl_3$) 0.99 (3H, t, *J* 7.5, CH_2CH_3), 1.98 (2H, app pentet, *J* 7.5, CH_2CH_3), 3.16 (1H, br s, O*H*), 3.39 (2H, app q, *J* 5.5, 5.0, CH_2NH), 3.66 (2H, app t, *J* 5.0, CH_2OH), 5.79 (1H, br s, N*H*), 7.03 (1H, t, *J* 7.5, C=C*H*), 7.17–7.21 (2H, m, Ar–*H*), 7.35–7.46 (3H, m, Ar–*H*); δ_C($CDCl_3$) 13.4, 23.1, 43.4, 62.8, 128.6, 129.0, 130.2, 135.1, 135.8, 143.8, 168.8; *m*/*z* ($EI^{+\bullet}$) 219 (18, $M^{+\bullet}$), 159 (22, $M^{+\bullet}$–$HOCH_2CH_2NH^{\bullet}$), 77 (100%); HRMS (FAB^+) $C_{13}H_{18}NO_2$ [MH^+] requires 220.1332; found 220.1332.

(2*E*,4*E*)-*N*-(2-Hydroxyethyl)-2-isopropyl-2,4-hexadienamide 4i and (2*Z*,4*E*)-*N*-(2-hydroxyethyl)-2-isopropyl-2,4-hexadienamide 5. Reaction of *syn*-3-[(*E*)-3-hydroxy-2-isopropyl-4-hexenoyl]-1,3-oxazolidin-2-one **3i** (0.200 g, 0.83 mmol) with a 0.5 M solution of KHMDS in toluene (2.50 mL, 1.25 mmol) in THF (5 mL), according to general procedure C, gave the title compound (*E*,*E*)-**4i** (0.153 g, 0.78 mmol) in 93% yield and in 60% de which was purified through silica (pre-coated with silver nitrate) gel chromatography to afford the title compound (*E*,*E*)-**4i** (0.016 g, 0.08 mmol) in 10% yield as a pale oil, δ_H(300 MHz, $CDCl_3$) 1.20 (6H, d, *J* 7.0, $CH(CH_3)_2$), 1.83 (3H, dd, *J* 7.0, 1.5, CH=CHCH_3), 2.95 (1H, septet, *J* 7.0, $CH(CH_3)_2$), 3.20 (1H, br s, O*H*), 3.45 (2H, app dt, *J* 5.5, 4.0, CH_2NH), 3.74 (2H, app t, *J* 5.0, CH_2OH), 5.89 (1H, dq, *J* 13.0, 7.0, CH=C*H*CH_3), 6.21 (1H, br s, N*H*), 6.33 (1H, br d, *J* 10.5, C*H*–CH=$CHCH_3$), 6.39 (1H, ddq, *J* 13.0, 10.5, 1.5, CH–C*H*=$CHCH_3$); δ_C($CDCl_3$) 19.0, 21.8, 28.6, 42.8, 63.0, 126.6, 130.6, 135.2, 141.0, 172.5; *m*/*z* ($EI^{+\bullet}$) 197 (23, $M^{+\bullet}$), 182 (33, $M^{+\bullet}$–$CH_3^{\bullet}$), 169 (38, $M^{+\bullet}$–$CH_3CH^{\bullet}$), 154 (100, $M^{+\bullet}$–$(CH_3)_2CH^{\bullet}$), 137 (28, $M^{+\bullet}$–$HO(CH_2)_2NH^{\bullet}$), 109 (43, $M^{+\bullet}$–$HO(CH_2)_2NHCO^{\bullet}$), and its geometric isomer (*Z*,*E*)-**5** (0.015 g, 0.08 mmol) in 9% yield, δ_H(300 MHz, $CDCl_3$) 1.08 (6H, d, *J* 7.0, $CH(CH_3)_2$), 1.77 (3H, dd, *J* 7.0, 1.5, CH=CHCH_3), 2.64 (1H, septet, *J* 7.0, $CH(CH_3)_2$), 3.00 (1H, br s, O*H*), 3.53 (2H, app dt, *J* 5.5, 4.5, CH_2NH), 3.78 (2H, app t, *J* 5.0, CH_2OH), 5.79 (1H, dq, *J* 15.0, 7.0, CHCH=C*H*CH_3), 5.99 (1H, d, *J* 11.0, C*H*–CH=$CHCH_3$), 6.13 (1H, br s, N*H*), 6.28 (1H, ddq, *J* 15.0, 11.0, 1.5, CH–C*H*=$CHCH_3$).

(2*E*,4*E*)-*N*-(2-Hydroxyethyl)-2-methyl-5-phenyl-2,4-pentadienamide 4j. Reaction of *syn*-3-[(*E*)-3-hydroxy-2-methyl-5-phenyl-4-pentenoyl]-1,3-oxazolidin-2-one **4j** (0.275 g, 1.00 mmol) with a 0.5 M solution of KHMDS (3.00 mL, 1.50 mmol) in THF (5 mL), according to general procedure C, gave the title compound (*E*)-**4j** (0.223 g, 0.97 mmol) in 97% yield and in 60% de The crude product was purified for analysis by recrystallisation from hot ethyl acetate, to afford the title compound (*E*)-**4j** (0.147 g, 0.64 mmol) in 64% yield and >95% de as a white solid, mp 141–142 °C; ν_{max}(KBr disc)/cm^{-1} 3293 (br, OH), 3250 (br, NH), 1642 (C=O), 1585 (C=C), 1542 (C=O); δ_H(300 MHz, $CDCl_3$) 2.08 (3H, s, CH_3), 2.87 (1H, t, *J* 5.0, O*H*), 3.55 (2H, app q, *J* 5.5, 5.0, CH_2NH), 3.80 (2H, app q, *J* 5.0, 5.0, CH_2OH), 6.32 (1H, br s, N*H*), 6.83 (1H, d, *J* 15.0, C*H*–CH=CHPh), 7.01 (1H, d, *J* 11.0, CHCH=C*H*Ph), 7.10 (1H, dd, *J* 15.0, 11.0, CHC*H*=CHPh), 7.28–7.48 (5H, m, Ar–*H*); δ_C($CDCl_3$) 13.6, 43.3, 63.1, 124.0, 127.3, 128.9, 129.1, 129.9, 134.9, 137.0, 138.6, 170.5; *m*/*z* ($EI^{+\bullet}$) 231 (33, $M^{+\bullet}$), 171 (80, $MH^{+\bullet}$–$HOCH_2CH_2NH^{\bullet}$), 154 (78, $M^{+\bullet}$–$Ph^{\bullet}$), 141 (47, $M^{+\bullet}$–$PhCH^{\bullet}$), 128 (100, $M^{+\bullet}$–$PhCHCH^{\bullet}$), 115 (38%, $M^{+\bullet}$–$PhCHCHCH^{\bullet}$); HRMS (FAB^+) $C_{14}H_{18}NO_2$ [MH^+] requires 232.1332, found 232.1330.

3-{(2*R*,3*R*)-3-Hydroxy-3-[(4*R*)-4-isopropenyl-1-cyclohexen-1-yl]-2-methylpropanoyl}-1,3-oxazo lid-in-2-one 8a and 3-{(2*S*,3*S*)-3-hydroxy-3-[(4*R*)-4-isopropenyl-1-cyclohexen-1-yl]-2-methylpropanoyl}-1,3-oxazolidin-2-one 9a. Reaction of 3-propionyl-1,3-oxazolidin-2-one **2a** (0.500 g, 3.50 mmol) with a 0.5 M

solution of 9-BBN-OTf in hexanes (8.40 mL, 4.20 mmol), *N*,*N*-diisopropylethylamine (0.85 mL, 4.90 mmol) and L-(−)-perillaldehyde (0.60 mL, 3.85 mmol) in CH_2Cl_2 (20 mL), according to general procedure B, afforded after purification through silica gel chromatography (20% ethyl acetate–petrol) the title compounds **8a/9a** (0.656 g, 2.24 mmol) in 64% yield as a white solid, as a 1 : 1 mixture of diastereomers, mp 87–88 °C; ν_{max}(KBr disc)/cm^{-1} 3495 (s, OH), 1769 (C=O)$_{ox}$, 1691 (C=O); δ_H(300 MHz, $CDCl_3$) 1.13 (3H, d, *J* 6.0, CH_3, **8a**), 1.15 (3H, d, *J* 6.0, CH_3, **9a**), 1.38–1.55 (2H, m, Cy-*H*), 1.74 (6H, s, 2 × CH_3C=CH_2), 1.82–1.88 (2H, m, Cy-*H*), 1.92–2.06 (4H, m, Cy-*H*), 2.11–2.24 (4H, m, Cy-*H*), 2.76 (1H, s, O*H*, **8a**), 2.78 (1H, s, O*H*, **9a**), 3.75 (1H, m, C*H*CH$_3$, **8a**), 3.96–4.00 (1H, m, C*H*CH$_3$, **9a**), 4.05 (4H, app t, *J* 8.0, CH_2N), 4.35–4.45 (2H, m, C*H*OH), 4.44 (4H, app t, *J* 8.0, CH_2O), 4.70–4.76 (4H, m, CH_2=C), 5.80–5.83 (2H, m, C*H*=C); δ_C($CDCl_3$) 10.2, 10.9, 21.2, 21.3, 25.7, 26.0, 26.5, 27.7, 27.8, 30.6, 30.9, 40.4, 40.8, 41.2, 41.7, 43.1, 62.4, 68.4, 74.3, 74.6, 109.0, 109.1, 122.4, 123.0, 136.2, 136.7, 149.9, 150.2, 153.6, 177.5, 177.6; *m*/*z* (CI$^+$, NH_3) 311 (9, MNH_4^+), 294 (15, MH^+), 276 (40, M^+–OH), 161 (100), 144 (39%, MH^+–CHOHCy); HRMS (FAB$^+$) $C_{16}H_{24}NO_4$ [MH^+] requires 294.1700; found 294.1695.

3-(2*R*,3*S*,5*S*)-3-Hydroxy-2,5,9-trimethyl-8-decenoyl)-1,3-oxazolidin-2-one 8b and 3-(2*S*,3*R*,5*S*)-3-hydroxy-2,5,9-trimethyl-8-decenoyl)-1,3-oxazolidin-2-one 9b. Reaction of 3-propionyl-1,3-oxazolidin-2-one **2a** (0.300 g, 2.10 mmol) with a 0.5 M solution of 9-BBN-OTf in hexanes (5.03 mL, 2.52 mmol), *N*,*N*-diisopropylethylamine (0.51 mL, 2.94 mmol) and (*S*)-citronellal (0.42 mL, 2.31 mmol) in CH_2Cl_2 (10 mL), according to general procedure B, afforded after purification through silica gel chromatography (gradient, 20–30% ethyl acetate–petrol) the title compounds **8b/9b** (0.576 g, 1.94 mmol) in 93% yield as a low viscosity colourless oil, as a 1 : 1 mixture of diastereoisomers, ν_{max}(neat)/cm^{-1} 3502 (br, OH), 1771 (C=O)$_{ox}$, 1695 (C=O); δ_H(300 MHz, $CDCl_3$) 0.92 (6H, app t, *J* 7.0, CHCH_3, **8b** + **9b**), 1.05–1.28 (4H, m, Alk-*H*), 1.20 (3H, d, *J* 7.0, O=CCHCH_3, **8b**), 1.21 (3H, d, *J* 7.0, O=CCHCH_3, **9b**), 1.30–1.48 (4H, m, Alk-*H*), 1.60 (6H, s, CH=C(CH$_3$)CH_3), 1.68 (6H, s, CH=C(CH$_3$)CH_3), 1.54–1.70 (2H, m, C*H*CH$_3$), 1.92–2.08 (4H, m, CH_2CH=C(CH$_3$)$_2$), 2.73 (1H, d, *J* 2.3, OH, **8b**), 2.80 (1H, d, *J* 3.0, O*H*, **9b**), 3.73–3.83 (2H, m, O=CC*H*CH$_3$), 4.00–4.11 (6H, m, C*H*OH, CH_2N), 4.44 (4H, app t, *J* 8.0, CH_2O), 5.10 (2H, t, *J* 7.0, C*H*=C(CH$_3$)$_2$); δ_C($CDCl_3$) 10.6, 11.0, 18.1, 19.3, 20.6, 25.7, 25.9, 26.0, 26.1 (2C), 29.3, 29.6, 36.9, 38.3, 41.4, 41.5, 42.2 (2C), 42.9, 43.0, 62.3, 68.4, 69.6, 69.8, 125.1, 131.6, 131.6, 153.6, 153.6, 177.9, 178.0; *m*/*z* (EI$^+$) 297.2 (11, $M^{+\bullet}$), 143 (100%); HRMS (ES$^+$) $C_{16}H_{28}NO_4$ [MH^+] requires 298.2013; found 298.2009.

(2*R*,3*R*)-3-{3-[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-hydroxy-2-methylpropanoyl}-1,3-oxazol-idin-2-one 8c and (2*S*,3*S*)-3-{3-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-3-hydroxy-2-methylpropanoyl}-1,3-oxazolidin-2-one 9c. Reaction of 3-propionyl-1,3-oxazolidin-2-one **2a** (0.200 g, 1.40 mmol) with a 0.5 M solution of 9-BBN-OTf in CH_2Cl_2 (3.36 mL, 1.68 mmol), *N*,*N*-diisopropylethylamine (0.34 mL, 1.96 mmol) and (*R*)-(+)-2,2-dimethyl-1,3-dioxolane-4-carboxaldehyde (0.19 mL, 1.54 mmol) in hexanes (7 mL), according to general procedure B, afforded after purification through silica gel chromatography (gradient, 40–50% ethyl acetate–petrol) the title compounds **8c/9c** (0.222 g, 0.81 mmol) in 58% yield as a thick colourless oil, as a 2 : 1 mixture of diastereoisomers, ν_{max}(neat)/cm^{-1} 3447 (br, OH), 1771 (C=O)$_{ox}$, 1699 (C=O); δ_H(300 MHz, $CDCl_3$) 1.28 (3H, d, *J* 6.5, CHCH_3, **8c**), 1.34 (6H, s, CH$_3$), 1.38 (3H, d, *J* 6.5, CHCH_3, **9c**), 1.43 (6H, s, CH$_3$), 2.55 (1H, d, *J* 6.5, O*H*, **8c**), 3.11 (1H, d, *J* 3.0, O*H*, **9c**), 3.72–4.18 (10H, m, C*H*CH$_3$, C*H*OH, C*H*OH, 2 × CH_2O), 4.05 (4H, app t, *J* 7.5, CH_2N), 4.44 (4H, app t, *J* 7.5, CH_2O); δ_C($CDCl_3$) 11.2, 12.1, 25.6, 25.8, 26.8, 27.1, 39.5, 41.3, 43.1, 62.3, 62.4, 66.6, 67.8, 68.4, 72.0, 73.1, 75.6, 77.2, 109.8, 110.1, 153.2, 153.6, 175.6, 178.0; *m*/*z* (CI$^+$, NH_3) 291 (30%, MNH_4^+), 274 (46, MH^+), 256 (5, M^+–OH), 230 (20, MH^+–CO_2), 144 (13, MH^+–CHOHR), 105.0 (100%); HRMS (ES$^+$) $C_{12}H_{20}NO_6$ [MH^+] requires 274.1285, found 274.1282.

(*E*,*E*)-*N*-(2-Hydroxyethyl)-3-[(4*R*)-4-isopropenyl-1-cyclohexen-1-yl]-2-methyl-2-propenamide 10a. Reaction of the mixture of aldols **8a/9a** (0.100 g, 0.34 mmol) with a 0.5 M solution of KHMDS in toluene (2.05 mL, 1.02 mmol) in THF (4 mL), according to general procedure C, gave the title compound (*R*,*E*,*E*)-**10a** in 50% de. The crude mixture was purified by silica gel chromatography (60% ethyl acetate–petrol) to afford the title compound (*R*,*E*,*E*)-**10a** (0.043 mg, 0.17 mmol) in 51% isolated yield and >95% de as a white solid, $[\alpha]_D^{21}$ −72.2 (*c* 0.90, CH_2Cl_2); mp 67–69 °C; ν_{max}(KBr disc)/cm^{-1} 3300 (br, NH), 3292 (s, OH), 1634 (C=O), 1603 (C=C), 1538 (C=O); δ_H(300 MHz, $CDCl_3$) 1.35–1.48 (1H, m, Cy-*H*), 1.68 (3H, s, CH$_2$=CHCH_3), 1.75–1.84 (1H, m, Cy-*H*), 1.95 (3H, s, CH=CCH_3), 2.00–2.11 (2H, m, Cy-*H*), 2.16–2.24 (3H, m, Cy-*H*), 3.28 (1H, s, O*H*), 3.42 (2H, app q, *J* 5.0, CH_2NH), 3.68 (2H, app t, *J* 5.0, CH_2OH), 4.67 (2H, d, *J* 7.0, C=CH_2), 5.76 (1H, m, C=C*H*CH$_2$), 6.33 (1H, br s, N*H*), 6.66 (1H, s, CH$_3$C=C*H*); δ_C($CDCl_3$) 14.7, 21.2, 28.0, 29.4, 31.6, 40.8, 43.3, 62.9, 109.3, 128.5, 131.5, 134.6, 137.4, 149.7, 171.8; *m*/*z* (EI$^{+\bullet}$) 249 (16, $M^{+\bullet}$), 208 (11, $M^{+\bullet}$–$CH_3CH(CH_2)^{\bullet}$), 189 (10%, $M^{+\bullet}$–$HOCH_2CH_2NH^{\bullet}$), 121 (55%, Cy^+), 91 (100%); HRMS (ES$^+$) $C_{15}H_{24}NO_2$ [MH^+] requires 250.1802, found 250.1802.

(2*E*,5*S*)-*N*-(2-Hydroxyethyl)-2,5,9-trimethyl-2,8-decadienamide 10b. Reaction of aldols **8b/9b** (0.150 mg, 0.51 mmol) with a 0.5 M solution of KHMDS in toluene (1.52 mL, 0.76 mmol) in THF (3 mL), according to general procedure C, gave the title compound (*S*,*E*)-**10b** (0.121 mg, 0.48 mmol) in 60% de. The crude product was purified by silica gel chromatography (60% ethyl acetate–petrol) to afford the title compound (*S*,*E*)-**10b** (0.071 g, 0.28 mmol) in 55% yield and >95% de as a colourless oil, $[\alpha]_D^{21}$ +2.7 (*c* 2.61, CH_2Cl_2), ν_{max}(neat)/cm^{-1} 3402 (br, OH, NH), 1657 (C=O), 1615 (C=C), 1538 (C=O); δ_H(300 MHz, $CDCl_3$) 0.90 (3H, d, *J* 6.5, CHCH_3), 1.12–1.27 (1H, m, CH_AH_BCH$_2$CH=C(CH$_3$)$_2$), 1.30–1.42 (1H, m, CH$_A$$H_BCH_2$CH=C(CH$_3$)$_2$), 1.55–1.65 (1H, m, C*H*CH$_3$), 1.60 (3H, s, CH=C(CH_3)$_2$), 1.68 (3H, s, CH=C(CH_3)$_2$), 1.85 (3H, s, CH=CCH_3), 1.90–2.05 (2H, m, CH_2CH=C(CH$_3$)$_2$), 2.10–2.19 (2H, m, CH_2CH=CCH$_3$), 3.48 (2H, app q, *J* 5.5, 5.0, CH_2NH), 3.61 (1H, br s, O*H*), 3.72–3.76 (2H, m, CH_2OH), 5.07 (1H, t, *J* 7.0, C*H*=C(CH$_3$)$_2$), 6.41 (1H, br s, N*H*), 6.44 (1H, t, *J* 6.5, C*H*=C); δ_C($CDCl_3$) 13.2, 18.1, 20.0, 26.0, 26.1, 33.1, 36.1, 37.2, 43.1, 62.8, 124.9, 131.1, 131.8, 136.6, 171.0; *m*/*z* (EI$^+$) 253 (46, $M^{+\bullet}$), 238 (18, $M^{+\bullet}$–$CH_3^{\bullet}$), 193 (5, $M^{+\bullet}$–$HOCH_2CH_2NH^{\bullet}$), 170 (41, $M^{+\bullet}$–$(CH_3)_2C$=CHC$H_2CH_2^{\bullet}$), 109 (100%); HRMS (ES$^+$) $C_{15}H_{28}NO_2$ [MH^+] requires 254.2115; found 254.2112.

(*E*)-3-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-*N*-(2-hydroxyethyl)-2-methyl-2-propenamide 10c. Reaction of aldols **8c/9c** (0.100 g, 0.37 mmol) with a 0.5 M solution of KHMDS (1.10 mL, 0.55 mmol) in THF (2 mL), according to general procedure C, gave the title compound (*S*,*E*)-**10c** in 80% de. The crude mixture was purified by silica gel chromatography (70% ethyl acetate–petrol) to afford the title compound (*S*,*E*)-**10c** (0.035 g, 0.15 mmol) in 42% yield and >95% de as a colourless oil, $[\alpha]_D^{21}$ +4.5 (*c* 1.54, CH_2Cl_2); ν_{max}(neat)/cm^{-1} 3305 (br, OH, NH), 1668 (C=O), 1622 (C=C), 1538 (C=O); δ_H(300 MHz, $CDCl_3$) 1.41 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.93 (3H, d, *J* 1.2, C=C(CH_3)), 3.27 (1H, s, O*H*), 3.47 (2H, app q, *J* 5.0, CH_2NH), 3.61 (1H, app t, *J* 8.0, C$H_A$$H_B$O), 3.74 (2H, app t, *J* 5.0, CH_2OH), 4.15 (1H, dd, *J* 8.0, 6.0, CH$_A$$H_B$O), 4.84 (1H, td, *J* 8.0, 6.0, C*H*OCH=), 6.25 (1H, dq, *J* 8.0, 1.2, C*H*=C), 6.52 (1H, br s, N*H*); δ_C($CDCl_3$) 13.8, 26.2, 27.0, 43.0, 62.3, 69.2, 72.9, 110.1, 132.8, 135.1, 170.1; *m*/*z* (CI$^+$, iso-butane) 230 (98, MH^+), 214 (20, M^+–$CH_3^{\bullet}$), 172 (68, M^+–$(CH_3)_2CO$), 141 (63, M^+–$HOCH_2CH_2NHCO$), 88 (100%); HRMS (ES$^+$) $C_{11}H_{20}NO_4$ [MH^+] requires 230.1387; found 230.1389.

***syn*-3-(2-Hydroxyethyl)-5-methyl-6-phenyl-1,3-oxazinane-2,4-dione 16[27].** Reaction of *syn*-3-(3-hydroxy-2-methyl-3-phenylpropanoyl)-1,3-oxazolidin-2-one **3b** (0.150 g, 0.60 mmol) with a 1.0 M solution of Et_2Zn in toluene (0.06 mL, 0.06 mmol) in CH_2Cl_2 (3 mL), according to general procedure D, afforded the title compound *syn*-**16** (0.147 g, 0.58 mmol) in 97% yield and 95% de as a colourless oil, ν_{max}(neat)/cm^{-1} 3447 (br, OH), 1755 (C=O)$_{ox}$, 1703 (C=O); δ_H(300 MHz, $CDCl_3$) 1.01 (3H, d, *J* 7.5, CH_3), 2.17 (1H, s, O*H*), 2.99 (1H, qd, *J* 7.5, 3.5, C*H*CH$_3$), 3.75–3.82 (2H, m, CH_2OH), 3.97 (1H, app dt, *J* 14.0, 5.5, CH_AH$_B$N), 4.05 (1H, app dt, *J* 14.0, 5.5, CH$_A$$H_B$N), 5.62 (1H, d, *J* 3.5, C*H*Ph), 7.24–7.38 (5H, m, Ar–*H*); δ_C($CDCl_3$) 10.4, 41.5, 44.6, 61.2, 78.1, 126.0, 129.2, 129.4, 134.4, 152.4, 173.2; *m*/*z* (CI$^+$, NH_3) 267 (15, MNH_4^+), 206 (47, MH$^+$–CO_2), 105 (100%); HRMS (ES$^+$) $C_{13}H_{16}NO_4$ [MH$^+$] requires 250.1079, found 250.1081. Reaction of *syn*-1,3-oxazinane-2,4-dione **16** (0.100 g, 0.40 mmol) with a 0.5 M solution of KHMDS in toluene (0.91 mL, 0.6 mmol) in THF (3 mL), according to general procedure C, gave (*E*)-**4b** (0.068 g, 0.33 mmol) in 82% yield and in 95% de.

***syn*-3-(2-Hydroxyethyl)-5-isopropyl-6-[(*E*)-1-propenyl]-1,3-oxazinane-2,4-dione 17.** Reaction of *syn*-3-[(*E*)-3-hydroxy-2-isopropyl-4-hexenoyl]-1,3-oxazolidin-2-one **3i** (0.200 g, 0.83 mmol) with a 1.0 M solution of Et_2Zn in toluene (0.08 mL, 0.08 mmol) in CH_2Cl_2 (5 mL), according to general procedure D, afforded the title compound *syn*-**17** (0.129 g, 0.54 mmol) in 65% yield and >95% de as a colourless oil, ν_{max}(neat)/cm^{-1} 3430 (br, OH), 1755 (C=O)$_{ox}$, 1699 (C=O); δ_H(300 MHz, $CDCl_3$) 0.97 (3H, d, *J* 7.0, CH(CH_3)$_2$), 1.03 (3H, d, *J* 7.0, CH(CH_3)$_2$), 1.71 (3H, d, *J* 7.0, CH_3CH=CH), 1.97 (1H, t, *J* 5.5, O*H*), 2.10 (1H, m, *J* 7.0, 4.5, C*H*(CH$_3$)$_2$), 2.55 (1H, dd, *J* 7.0, 4.5, C*H*^{i}Pr), 3.74 (2H, app dt, *J* 5.5, 5.5, CH_2OH), 3.94–3.98 (2H, m, CH_2N), 4.92 (1H, app t, *J* 7.0, C*H*CH=CHCH$_3$), 5.47 (1H, dd, *J* 15.0, 7.0, CH$_3$CH=C*H*), 5.91 (1H, dq, *J* 15.0, 7.0, CH$_3$C*H*=CH); δ_C($CDCl_3$) 17.0, 19.7, 20.3, 24.8, 43.2, 49.5, 60.1, 76.6, 122.1, 132.7, 151.3, 169.7; *m*/*z* (EI$^{+\bullet}$) 241 (41, M$^{+\bullet}$), 198 (100%, M$^{+\bullet}$–$CO_2^{\bullet}$); HRMS (ES$^+$) $C_{12}H_{19}NO_4$ [MH$^+$] requires 241.1314, found 241.1313. Reaction of *syn*-1,3-oxazinane-2,4-dione **17** (0.010 g, 0.04 mmol) with a 0.5 M solution of KHMDS in toluene (0.09 mL, 0.06 mmol) in THF (3 mL), according to general procedure C, gave (2*E*,4*E*)-**4i** (0.007 g, 0.035 mmol) in 88% yield and in 60% de.

***anti*-3-(3-Hydroxy-2-methyl-3-phenylpropanoyl)-1,3-oxazolidin-2-one 18[27].** Magnesium chloride (0.033 g, 0.35 mmol), triethylamine (0.97 mL, 6.99 mmol), benzaldehyde (0.43 mL, 4.19 mmol) and trimethylsilyl chloride (0.67 mL, 5.24 mmol) were added to a solution of 3-propionyl-1,3-oxazolidin-2-one **2a** (0.500 g, 3.50 mmol) in ethyl acetate (7 mL). The reaction mixture was stirred for 24 hours, and then filtered through a plug of silica which was then washed with Et_2O (10 ml). The organic layer was concentrated *in vacuo*, before addition of methanol (2 drops) and trifluoroacetic acid. The solvent was then removed before purification through silica gel chromatography (30% ethyl acetate–petrol) to afford the title compound *anti*-**18** (0.290 g, 1.16 mmol) in 33% yield as a white crystalline solid, mp 102–104 °C (lit,[27] 107–107.5 °C); ν_{max}(KBr disc)/cm^{-1} 3446 (s, OH), 1783 (C=O)$_{ox}$, 1665 (C=O); δ_H(300 MHz, $CDCl_3$) 1.05 (3H, d, *J* 7.0, CH_3), 2.87 (1H, d, *J* 5.0, O*H*), 4.00–4.06 (2H, m, CH_2N), 4.28 (1H, dq, *J* 8.5, 7.0, C*H*CH$_3$), 4.36–4.45 (2H, m, CH_2O), 4.78 (1H, dd, *J* 8.5, 5.0, C*H*OH), 7.26–7.43 (5H, m, Ar–*H*); δ_C($CDCl_3$) 15.2, 43.1, 44.8, 62.4, 77.5, 127.1, 128.5, 129.0, 142.1, 153.9, 176.9; *m*/*z* (CI$^+$, NH_3) 267 (94, MNH_4^+), 250 (48, MH$^+$), 105.1 (100%); HRMS (ES$^+$) $C_{13}H_{16}NO_4$ [MH$^+$] requires 250.1079, found 250.1079. Reaction of *anti*-aldol **18** (0.100 g, 0.4 mmol) with a 0.5 M solution of KHMDS in toluene (1.20 mL, 0.6 mmol) in THF (3 mL), according to general procedure C, gave (*E*)-**4b** (0.061 g, 0.3 mmol) in 74% yield and in 95% de.

***anti*-3-(2-Hydroxyethyl)-5-methyl-6-phenyl-1,3-oxazinane-2,4-dione 19[27].** Reaction of *anti*-3-(3-hydroxy-2-methyl-3-phenylpropanoyl)-1,3-oxazolidin-2-one **18** (0.050 g, 0.20 mmol) with a 1.0 M solution of Et_2Zn in toluene (0.02 mL, 0.02 mmol) in CH_2Cl_2 (1 mL), according to general procedure D, afforded the title compound *anti*-**19** (0.047 g, 0.19 mmol) in 96% yield and >95% de as a white solid, ν_{max}(neat)/cm^{-1} 3435 (br, OH), 1755 (C=O)$_{ox}$, 1694 (C=O); δ_H(300 MHz, $CDCl_3$) 1.02 (3H, d, *J* 7.0, CH_3), 2.21 (1H, br s, O*H*), 2.89 (1H, qd, *J* 11.5, 7.0, C*H*(CH$_3$)), 3.77–3.80 (2H, app t, *J* 5.5, CH_2OH), 3.94 (1H, ddd, *J* 14.0, 6.0, 4.5, CH_AH$_B$N), 4.06 (1H, app dt, *J* 14.0, 5.5, CH$_A$$H_B$N), 5.04 (1H, d, *J* 11.5, C*H*Ph), 7.24–7.38 (5H, m, Ar–*H*); δ_C($CDCl_3$) 10.1, 40.4, 43.5, 59.6, 80.5, 126.1, 127.9, 128.7, 134.2, 151.1, 170.5; *m*/*z* (CI$^+$, NH_3) 267 (MNH_4^+, 100%), 250 (46, MH$^+$), 208 (55), 206 (87%, MH$^+$–CO_2); HRMS $C_{13}H_{16}NO_4$ (ES$^+$) [MH$^+$] requires 250.1079, found 250.1077. Reaction of *anti*-1,3-oxazinane-2,4-dione **19** (0.020 g, 0.075 mmol) with a 0.5 M solution of KHMDS in toluene (0.18 mL, 0.012 mmol) in THF (3 mL), according to general procedure C, gave (*E*)-**4b** (0.012 g, 0.006 mmol) in 80% yield and in 95% de.

(*E*)-3-Cyclohexyl-2-isopropyl-2-propenoic acid 26a[38]. Hydrolysis of (*E*)-3-cyclohexyl-*N*-(2-hydroxyethyl)-2-isopropyl-2-propenamide **4a** (0.053 g, 0.22 mmol) in 6.0 M HCl (2 mL), according to general procedure E, afforded the title compound (*E*)-**26a** (0.043 g, 0.22 mmol) in 99% yield and >95% de as a colourless oil, ν_{max}(neat)/cm^{-1} 3450 (br, OH), 1677 (C=O), 1621 (C=C)$_{conj}$; δ_H(300 MHz, $CDCl_3$) 0.90–1.30 (6H, m, Cy-*H*), 1.13 (6H, d, *J* 7.0, CH(CH_3)$_2$), 1.52–1.72 (4H, m, Cy-*H*), 2.33 (1H, dtt, *J* 10.5, 10.0, 3.5, C*H*), 2.84 (1H, septet, *J* 7.0, C*H*(CH$_3$)$_2$), 6.54 (1H, d, *J* 10.0, C*H*=CCH$_3$), 10.26 (1H, br s, COO*H*); δ_C($CDCl_3$) 20.2, 24.5, 26.4, 31.3, 31.9, 36.4, 134.1, 148.2, 172.7.; *m*/*z* (EI$^{+\bullet}$) 197.3 (15%, MH$^{+\bullet}$), 196.3 (15%, M$^{+\bullet}$); HRMS (ES$^+$) $C_{12}H_{20}O_2$ [MH$^+$] requires 196.1458; found 196.1454.

(*E*)-2-Methyl-3-phenyl-2-propenoic acid 26b. Hydrolysis of (*E*)-*N*-(2-hydroxyethyl)-2-methyl-3-phenyl-2-propenamide **4b** (0.048 g, 0.23 mmol) in 6.0 M HCl (3 mL), according to general procedure E, afforded the title compound (*E*)-**26b** (0.036 g, 0.22 mmol) in 95% yield and >95% de as a colourless oil, ν_{max}(neat)/cm^{-1} 3445 (br, OH), 1668 (C=O), 1616 (C=C)$_{conj}$; δ_H(300 MHz, $CDCl_3$) 2.08 (s, 3H, CH=CCH_3), 7.26–7.36 (5H, m, Ar–*H*), 7.77 (1H, s, C*H*=CCH$_3$), 11.36 (1H, br s, COO*H*); δ_C($CDCl_3$) 12.7, 126.5, 127.4, 127.7, 128.8, 134.5, 140.1, 173.4; *m*/*z* (EI$^+$) 162.1 (68%, M$^{+\bullet}$), 161.0 (36%, M$^{+\bullet}$–H$^{\bullet}$), 117.2 (58%, M$^{+\bullet}$–COOH$^{\bullet}$); HRMS (ES$^+$) $C_{10}H_{10}O_2$ [MH$^+$] requires 162.0675; found 162.0672.

(*E*)-2-Methylpenten-2-oic acid 26c. Hydrolysis of (*E*)-*N*-(2-hydroxyethyl)-2-methyl-2-pentenamide **4c** (0.300 g, 1.91 mmol) in 6.0 M HCl (5 mL), according to general procedure E, afforded the title compound (*E*)-**26c** (0.230 g, 2.02 mmol) in 91% yield and >95% de as a low-melting white solid, ν_{max}(neat)/cm^{-1} 3429 (br, OH), 1700 (C=O), 1646 (C=C); δ_H(300 MHz, $CDCl_3$) 0.99 (3H, t, *J* 7.5, CH$_2$CH_3), 1.76 (3H, d, *J* 1.0, CH=CCH_3), 2.14 (2H, app pentet, *J* 7.5, CH_2CH$_3$), 6.83 (1H, tq, 7.5, 1.0, C*H*=CCH$_3$), 11.70 (1H, br s, COO*H*); δ_C($CDCl_3$) 12.2, 13.2, 22.6, 126.8, 147.2, 174.3.

(*E*)-2-Benzyl-2-decenoic acid 26d. Hydrolysis of (*E*)-2-benzyl-*N*-(2-hydroxyethyl)-2-decenamide **4d** (0.200 g, 0.58 mmol) in 6.0 M HCl (5 mL), according to general procedure E, afforded the title compound (*E*)-**26d** (0.143 mg, 0.55 mmol) in 95% yield and >95% de, δ_H(300 MHz, $CDCl_3$) 0.80 (3H, t, *J* 7.0, CH_3), 1.12–1.25 (8H, m, Alk-*H*), 1.29–1.38 (2H, m, CH_2CH$_2$CH=C), 2.19 (2H, app q, *J* 7.5, CH_2CH=C), 3.58 (2H, s, CH_2Ph), 6.70 (1H, s, C*H*=CBn); 6.97–7.17 (5H, m, Ar–*H*); 10.70 (1H, br s, COO*H*); δ_C($CDCl_3$) 13.0, 21.6, 27.5, 28.0, 28.2, 28.3, 30.7, 31.2, 125.0, 127.2, 127.3, 129.2, 138.5, 146.1, 171.9; *m*/*z* (EI$^{+\bullet}$) 260.3 (66, M$^{+\bullet}$), 242 (9, M$^{+\bullet}$–H_2O), 161 (14, M$^{+\bullet}$–CH$_3$(CH$_2$)$_6^{\bullet}$), 91 (100%); HRMS (ES$^+$) $C_{17}H_{28}NO_2$ [MNH_4^+] requires 278.2120; found 278.2118.

(2*E*,4*E*)-2-Methyl-5-phenyl-2,4-pentadienoic acid 27[39]. Hydrolysis of (*E*,*E*)-*N*-(2-hydroxyethyl)-2-methyl-5-phenyl-2,4-pentadienamide **4j** (0.200g, 0.85 mmol) in 6.0 M HCl (5 mL), according to general procedure E, afforded the title compound (*E*,*E*)-**27** (0.158 g, 0.45 mmol) in 77% yield and >95% de as a pale brown solid, mp 158–160 °C (lit,[39] 160.0–162.5 °C); ν_{max}(KBr disc)/cm^{-1} 3445 (br, OH), 1683 (C=O), 1622 (C=C)$_{conj}$; δ_H(300 MHz, $CDCl_3$) 1.98 (3H, d, *J* 1.1, C*H*$_3$), 6.83 (1H, d, *J* 15.5, CHCH=C*H*Ph), 7.00 (1H, dd, *J* 15.5, 11.5, CH–C*H*=CHPh), 7.17–7.45 (6H, m, C*H*–CH=CHPh, Ar–H), 11.00 (1H, br s, COO*H*); δ_C($CDCl_3$) 11.5, 122.7, 125.4, 126.2, 127.8, 127.9, 135.4, 139.2, 139.6, 173.0; *m*/*z* (EI$^{+\bullet}$) 188 (33, M$^{+\bullet}$), 143 (62, M$^{+\bullet}$–COOH$^{\bullet}$), 128 (80, M$^{+\bullet}$–COOH–CH$_3$), 115 (100%, M$^{+\bullet}$–C(CH$_3$)COOH–H$^+$); HRMS (ES$^+$) $C_{12}H_{16}NO_2$ [MNH_4^+] requires 206.1176; found 206.1175.

2-[(*E*)-1-Methyl-2-phenyl-1-ethenyl]-4,5-dihydro-1,3-oxazole 28. Reaction of (*E*)-*N*-(2-hydroxyethyl)-2-methyl-3-phenyl-2-propenamide **4b** (0.570 g, 2.78 mmol) with thionyl chloride (0.89 mL, 12.20 mmol) in CH_2Cl_2 (15 mL), according to general procedure F, gave the title compound (*E*)-**28** (0.503 g, 2.69 mmol) in 97% yield and >95% de as a pale yellow oil, ν_{max}(neat)/cm^{-1} 1707 (C=N), 1640 (C=C); δ_H(300 MHz, $CDCl_3$) 2.21 (3H, d, *J* 1.5, CH=CC*H*$_3$), 4.01 (2H, app t, *J* 9.5, C*H*$_2$N), 4.36 (2H, app t, *J* 9.5, C*H*$_2$O), 7.12 (1H, d, *J* 1.5, CH=C(Me)), 7.35–7.40 (5H, m, Ar–*H*); δ_C($CDCl_3$) 15.4, 55.4, 67.9, 125.7, 128.2, 128.7, 129.9, 135.6, 136.7, 167.3; *m*/*z* (EI$^{+\bullet}$) 187 (27, M$^{+\bullet}$), 186 (100, M$^{+\bullet}$–H$^{\bullet}$), 129 (7, M$^{+\bullet}$–OCH$_2$CH$_2$N), 115 (25%, CH_3CCPh^+); HRMS (ES$^+$) $C_{12}H_{13}NO$ [MH^+] requires 187.0997; found 187.0998.

2-[(*E*)-1-Methyl-1-butenyl]-4,5-dihydro-1,3-oxazole 29. Reaction of (*E*)-*N*-(2-hydroxyethyl)-2-methyl-2-pentenamide **4c** (0.112 g, 0.71 mmol) with thionyl chloride (0.26 mL, 3.57 mmol) in CH_2Cl_2 (4 mL), according to general procedure F, gave the title compound (*E*)-**29** (0.087 g, 0.63 mmol) in 88% yield and >95% de as a colourless oil, ν_{max}(neat)/cm^{-1} 1700 (C=N), 1653 (C=C); δ_H(300 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.6, CH$_2$C*H*$_3$), 1.85 (3H, s, CH=CC*H*$_3$), 2.12 (2H, app pentet, *J* 7.5, C*H*$_2$CH$_3$), 3.86 (2H, t, *J* 9.5, C*H*$_2$N), 4.20 (2H, t, *J* 9.5, C*H*$_2$O), 6.34 (1H, t, *J* 7.4, C*H*=CCH$_3$); δ_C($CDCl_3$) 13.5, 13.7, 22.1, 55.1, 67.5, 123.9, 140.1, 166.8; *m*/*z* (EI$^{+\bullet}$) 139 (55%, M$^{+\bullet}$), 124 (100%, M$^{+\bullet}$–CH$_3^{\bullet}$); HRMS (ES$^+$) $C_8H_{14}NO$ [MH^+] requires 140.1070; found 140.1072.

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which corresponds to the structure of aldol **3i** reported in this paper. Furthermore, we were unable to reproduce the >95% de reported for the elimination reaction of *syn*-aldol **3i** to afford (*E*)-amide **4i**, and have concluded that this value is also incorrect, and must have arisen from unintentional fractional crystallisation of the crude reaction product prior to ^{1}H NMR spectroscopic analysis.
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