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# Alkynes to (*E*)-enolates using tandem catalysis: stereoselective *anti*-aldol and *syn*-[3,3]-rearrangement reactions

Neil P. Grimster [a], Donna A.A. Wilton [a], Louis K.M. Chan [a], Christopher R.A. Godfrey [b], Clive Green [c], Dafydd R. Owen [d], Matthew J. Gaunt [a,*]

[a] *Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, United Kingdom*
[b] *Syngenta Crop Protection, Münchwilen AG, Schaffhauserstrasse, WT-810.3.18, CH-4332 Stein, Switzerland*
[c] *AstraZeneca, Alderley Park, Macclesfield, Cheshire SK10 4TF, United Kingdom*
[d] *Pfizer Global Research and Development, Sandwich, Kent CT13 9NJ, United Kingdom*

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ABSTRACT

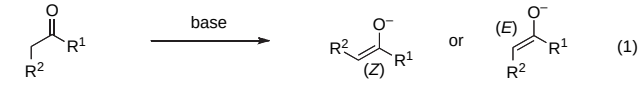
A new tandem catalysis strategy that transforms alkyne derivatives to (*E*)-enol-equivalents followed by stereoselective *anti*-selective aldol coupling or *syn*-selective [3,3]-rearrangement transformations is reported. The mechanism is thought to proceed through an interchanging series of Lewis acid and Brønsted acid catalyzed reactions via the intermediacy of a ketiminum ion species.



## 1. Introduction

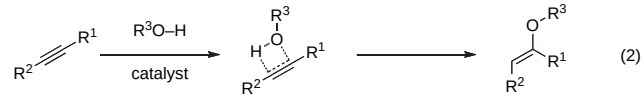
The enolate and its derivatives represent the most important reactive intermediate in synthetic organic chemistry.[1] The classical formation of enolates or enols is realized directly from the corresponding carbonyl compound via base mediated deprotonation or acid induced enolization, respectively (Eq. 1); this can often be controlled to form (*E*) or (*Z*) geometric isomers, depending on the nature of the carbonyl, or the conditions employed. The enolization event is controlled through a mix of steric and electronic factors that requires careful selection of reaction conditions. Recent advances have focused on the development of catalytic and asymmetric enolate chemistry, and have led to a number of important advances in this field.[2] A particular challenge for enolate chemistry is the generation and direct transformation of (*E*)-enolates derived from amides. A solution to this problem would have significant utility in synthesis. Herein, we disclose our initial studies towards the catalytic and stereoselective formation and reaction of (*E*)-enolate equivalents from alkynes (Eq. 2). This strategy uses an interchanging series of Lewis and Brønsted acid catalyzed processes (Eq. 3), and facilitates the *syn*-addition of an alcohol across an ynamide to form the (*E*)-enolate equivalent. This multi-catalysis system can also catalyze further transformations, and here we detail the development of catalytic stereoselective *anti*-aldol process and the demonstration of a *syn*-selective [3,3]-sigmatropic rearrangement reaction (Eq. 4).[3]

**Conventional enolate formation: carbonyls to enolates**



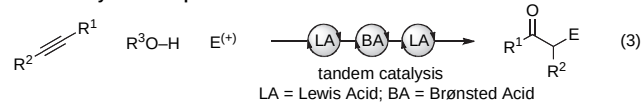

(1)

**New strategy for catalytic enol formation: alkynes to enolates**



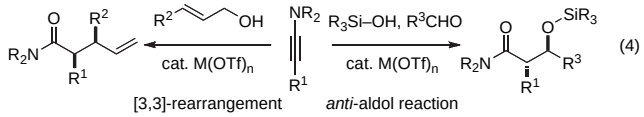

(2)

**Tandem catalysis concept**




(3)

**Applications of tandem catalysis strategy - this study**




(4)

* Corresponding author. Tel.: +44 (0)1223 336 318; fax: +44 (0)1223 336 362; e-mail address: mjg32@cam.ac.uk (M.J. Gaunt).

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## 2. Results and discussion

Central to our hypothesis for the 'enolization' of alkynes was the realization that ynamides possess the same overall oxidation state as an enol-aminal, and that the addition of an O–H group across the triple bond would reveal the enol functionality (Eq. 2). The catalyzed hydration of alkynes to ketones is a relatively well-known transformation[4] and yet, there are few examples of the direct intermolecular interception of the enol intermediate to facilitate further reactions.[5] Our first task was to design a system that would catalyze (a) the (*E*)-selective hydroalkoxylation of an ynamide, and (b) subsequent transformation of the enol derivative.[6] Guided by the ynamide **1** reactivity,[7] we speculated that the combination of a Lewis acid and protic nucleophile would generate a highly acidic species that could protonate the ynamide under mild conditions.[8]

To test this hypothesis, we treated ynamide **1a** with *i*-PrOH in the presence of $Zn(OTf)_2$ in $CH_2Cl_2$ at room temperature. Unfortunately, the only product observed was the amide resulting from hydrolysis of ynamide. However, on use of a larger oxazolidinone **1b**, we could observe the enol-aminal (*int*-**1b**). Importantly, NOE correlation revealed that the enol was of (*E*)-geometry, confirming the *syn*-addition process outlined in our enolization blueprint (Fig. 1).

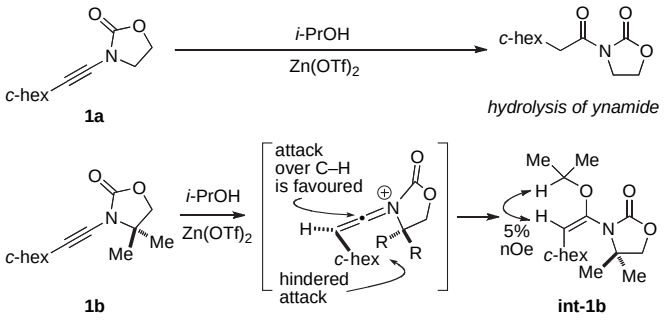


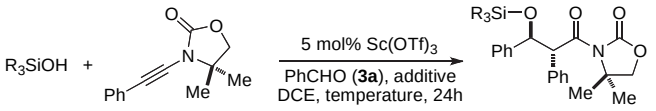

**Figure 1.** Initial investigation into the catalytic formation of (*E*)-enol-equivalents from ynamide **1**.

To rationalize this event, we propose that trifluoromethansulfonic acid (TfOH) is generated as a result of combining $Zn(OTf)_2$ in *i*-PrOH. This acid protonates the ynamide forming a ketimium species that undergoes selective attack over the C–H bond to form the (*E*)-enol derivative.[9] In monitoring this reaction by $^{19}F$ NMR spectroscopy we are able to detect the formation of TfOH, supporting our hypothesis for a multi-catalysis system.[3,8,10] To exploit the catalytic formation of this (*E*)-enol-equivalent, we considered its combination with an aldol-type transformation. Such a process would potentially enable a catalytic *anti*-aldol reaction, whose asymmetric variant would represent an important advance in this area.[1a,11] We selected $Ph_3Si$–OH **2a** as the protic nucleophile for the activation strategy as this would generate the corresponding enol-silane on reaction with the ynamide **1**. Subsequent tandem aldol reaction, through a Lewis acid mediated Mukaiyama-type mechanism, would potentially form the *anti*-aldol product **4**.

Our optimization with $Ph_3Si$–OH **2a**, phenyl-ynamide **1c** and benzaldehyde **3a** revealed that $Sc(OTf)_3$ was the best catalyst for this process, and that 1,2-dichloroethane (DCE) was the optimal solvent, delivering the aldol product in favour of the *anti*-isomer **4a** (Table 1, entry 1).

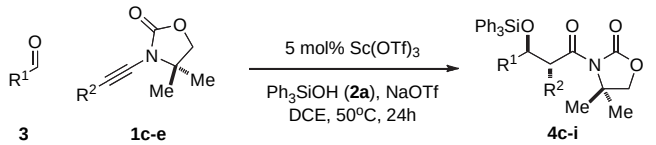
An increase in yield was observed upon addition of 1 equiv of NaOTf, resulting in an isolated yield of 73% (entry 2); further improvements were observed when the temperature of the reaction was increased to 50 °C, affording 80% of the desired aldol product (entry 3). It is possible that the NaOTf additive moderates the formation of TfOH (essentially buffering the reaction and minimizing the TfOH catalyzed decomposition). The diastereomeric ratio (dr) of the reaction could be improved by changing the nature of the silanol, with *i*-$Pr_3Si$–OH giving the highest selectivity for the reaction between ynamide **1c** and benzaldehyde **3a** (entry 4). In our initial assessment of the reaction scope we found that a range of substrates were suitable for this process (Table 2). Pleasingly, alkyl ynamide ($R^2$=Me **1d**) afforded *anti*-propionate aldol product **4c** with benzaldehyde in 54% yield (Table 2, entry 1).

**Table 1**
Optimization of the *anti*-aldol reaction




| Entry | Silanol **2** | Additive | Temp °C | Yield % | dr (*anti*/*syn*) |
|---|---|---|---|---|---|
| 1 | $Ph_3SiOH$ **2a** | — | rt | 51 | 67:33 |
| 2 | $Ph_3SiOH$ **2a** | NaOTf | rt | 73 | 67:33 |
| 3 | $Ph_3SiOH$ **2a** | NaOTf | 50 °C | 80 | 67:33 |
| 4 | *i*-$Pr_3SiOH$ **2b** | NaOTf | 50 °C | 65 | 80:20 |

**Table 2**
Scope of the *anti*-aldol reaction




| Entry | $R^1$ | $R^2$ | Yield % | dr (*anti*/*syn*) |
|---|---|---|---|---|
| 1 | Ph | Me | 54 (**4c**) | 67:33 |
| 2 | Ph | *n*-$C_6H_{13}$ | 62 (**4d**) | 80:20[b] |
| 3 | 2,6-$(OMe)_2C_6H_3$ | *n*-$C_6H_{13}$ | 66 (**4e**) | 83:17 |
| 4 | *n*-$C_3H_7$ | Ph | 57 (**4f**) | 86:14[b] |
| 5 | Ph | Ph | 80 (**4a**) | 67:33 |
| 6 | *i*-$C_3H_7$ | Ph | 73 (**4g**) | >95:5 |
| 7 | *c*-$C_6H_{11}$ | Ph | 72 (**4h**) | >95:5 |
| 8 | (±) Ph, Me | Ph | 43 (**4i**) | >95:5[a,b] |

[a] Felkin–Ahn/*anti*-Felkin–Ahn (3:1) isomers observed by $^1H$ NMR spectroscopy of the crude reaction mixture.
[b] Relative stereo-configuration of the *anti*-aldol products were confirmed by X-ray crystallography analysis (see Experimental for details).

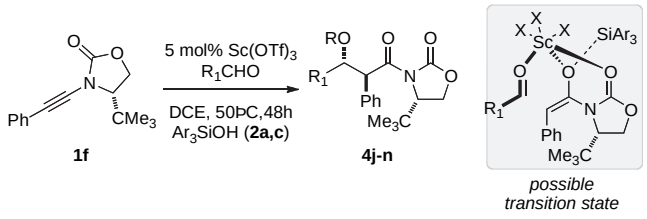
An improved dr was observed in cases when *n*-hexyl ynamide ($R^2$=*n*-Hex **1e**) was employed (entries 2 and 3). Unbranched alkyl aldehydes, such as butanal, gave the desired *anti*-aldol product **4f** in reasonable yield with 86:14 dr (entry 4). Reactions with α-branched aldehydes delivered the *anti*-aldol products **4g**–**i** in excellent dr (>95:5) and good yields (entries 6–8). It is notable that the silyl group is transferred to the hydroxyl during the reaction, providing a convenient concomitant hydroxyl protection feature. When α-phenylpropionaldehyde was employed, the reaction afforded a reasonable yield of **4i** (>95:5 *anti*/*syn*) as a 3:1 mixture of Felkin–Ahn to *anti*-Felkin–Ahn isomers (entry 8). In most cases, the *anti*-aldol isomer was crystalline, thereby providing a convenient method of separation and also providing proof of stereochemistry.

We next turned our attention to the investigation of an asymmetric process, and in particular to the auxiliary controlled *anti*-aldol reaction. Evans and co-workers have demonstrated that a Lewis acid catalyzed process can afford high dr using aromatic aldehydes.[11a,b] Interestingly, this reaction is proposed to occur

through a (*Z*)-enolate equivalent and boat-type transition state. Kobayashi et al. have also shown that diastereoselective aldol reactions with *N*-Boc amides proceed with excellent selectivity and yield.[11c]

In considering an asymmetric process, we found that the *anti*-aldol reaction between chiral ynamide **1f** (derived from (*S*)-*tert*-leucine), **2a** and *iso*-butanal proceeded in 44% yield and 94:6 dr (*anti*/sum of all other isomers, **4j**), under the optimal conditions (Table 3). However, when we changed the protic nucleophile to (*p*-F-$C_6H_4$)$_3$Si–OH **2c**, we found that the aldol reactions proceeded with excellent selectivity (>95:5 dr) in favour of the *anti*-diastereoisomer with both branched and unbranched alkyl aldehydes (**4k**-**n**). In contrast to $Ph_3Si$–OH, the use of (*p*-F-Ph)$_3$Si–OH **2c** results in cleavage of the silyl ether under the reaction conditions employed.

**Table 3**
Asymmetric *anti*-aldol reaction with aliphatic aldehydes




| Entry | $R_1$ | Ar | R | Yield % | dr (*anti*/*syn*) |
|---|---|---|---|---|---|
| 1 | *i*-$C_3H_7$ | Ph (**2a**) | $Ph_3Si$ | 44 (**4j**) | 94:6 |
| 2 | *i*-$C_3H_7$ | *p*-F-Ph (**2c**) | H | 52 (**4k**) | >95:5[a] |
| 3 | *c*-$C_6H_{11}$ | (**2c**) | H | 50 (**4l**) | >95:5 |
| 4 | *n*-$C_3H_7$ | (**2c**) | H | 50 (**4m**) | >95:5 |
| 5 | $(CH_2)_2$Ph | (**2c**) | H | 61 (**4n**) | >95:5 |

[a] Absolute stereo-configuration of the *anti*-aldol product was confirmed by X-ray crystallography analysis (see Experimental for details).

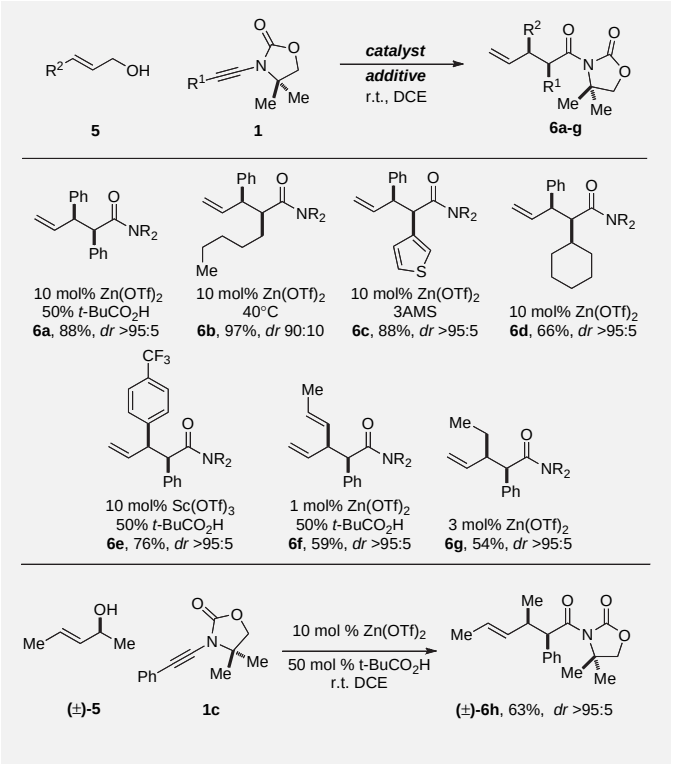
In order to further explore the capacity of the catalytic ynamide-to-enol transformation, we also investigated a [3,3]-sigmatropic process, based on the Ficini modification of the Claisen rearrangement.[12] The transformation involves the union of an ynamine and an allylic alcohol, followed by thermal rearrangement. Hsung recently reported that a sulfonic acid catalyzed rearrangement can be effected under thermal conditions at temperatures >80 °C.[13] In line with our hypothesis, we envisaged that both 'enol' formation and the rearrangement could be facilitated at ambient temperature.[14]

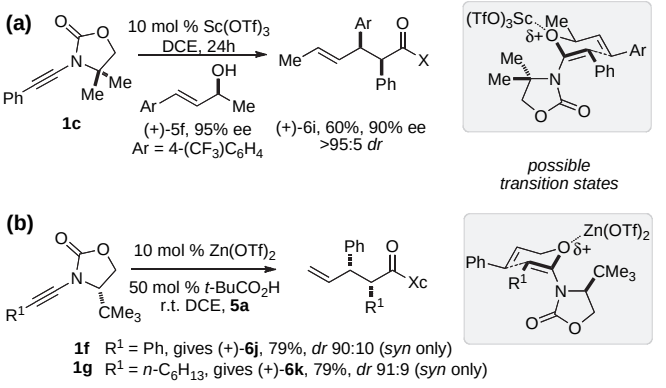
A similar screen of conditions to that of the aldol process identified optimal parameters comprising reaction of **5** ($R^2$=Ph) and **1c** in the presence of 1 mol % $Zn(OTf)_2$ and 50 mol % PivOH as the additive, resulting in 88% yield of **6a** (>95:5 dr) after 24 h at room temperature (Table 4). We also found that 1 mol % of $Sc(OTf)_3$ catalyzes the reaction with similar outcome.

We tested a range of substituted 1° and 2° allylic alcohols **5** and ynamides **1** under our optimized reaction conditions (Table 4) and showed that aryl ($R^1$, $R^2$), heteroaryl ($R^1$), alkenyl ($R^2$) and alkyl ($R^1$, $R^2$) substituents could be accommodated on both the ynamide ($R^1$) and allylic alcohol ($R^2$) portions of the molecule. In most cases diastereoselectivities (in favour of the *syn*-isomer) were excellent.

When enantioenriched (+)-**5f** was subjected to our standard reaction conditions, we found that the rearrangement took place with transposition of chirality from the allylic alcohol (+)-**5f** to the product (+)-**6i** (Scheme 1a). Using the ynamides **1f**–**g**, we found that rearrangement proceeded with good stereocontrol to afford only the *syn* products **6j**–**k** with good dr (Scheme 1b).[15] While we cannot fully rationalize the origin of stereoinductions, the observed outcome is consistent with a chair transition state and non-chelated auxiliary.

**Table 4**
Scope of catalytic [3,3]-rearrangment reaction




**Scheme 1.** Asymmetric [3,3]-sigmatropic rearrangement.

In summary, we have developed a new tandem catalysis strategy that transforms alkyne derivatives to (*E*)-enol-equivalents. Furthermore, catalytic stereoselective *anti*-selective aldol couplings and *syn*-selective [3,3]-rearrangement transformations can be effected through this tandem process. The mechanism is thought to proceed through an interchanging series of Lewis acid and Brønsted acid catalyzed reactions via the intermediacy of a ketiminum ion species. Further investigations into a catalytic enantioselective transformation are ongoing.

## 3. Experimental section

### 3.1. General experimental

All reagents were purchased at the highest commercial quality. Ynamides were synthesized according to literature procedure.[16] Reactions were carried out using oven dried glassware and under

an atmosphere of nitrogen unless otherwise stated. 1,2-Dichloroethane was freshly distilled over calcium hydride before use. All reactions were monitored by TLC carried out on glass precoated (0.25 mm) with Merck silica gel 60 $F_{254}$ or from $^1$H NMR spectra taken from reaction samples. Flash column chromatography was performed with Merck silica gel 60 (230–400 mesh).

$^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were determined on a Bruker DPX 400 MHz spectrometer operating at 400, 100 and 376 MHz, respectively. Chemical shifts ($\delta$) for $^1$H NMR, $^{13}$C NMR are quoted relative to residual solvent (chloroform, $\delta$=7.26 ppm for $^1$H and $\delta$=77.0 for $^{13}$C of chloroform-$d_1$) and chemical shifts ($\delta$) for $^{19}$F NMR are quoted relative to fluorobenzene ($\delta$=0.0). Coupling constants ($J$) are corrected and quoted to the nearest 0.1 Hz. DEPT135 and 2-dimensional experiments (COSY, HMBC and HMQC) were used to support assignments were appropriate, but are not included. IR spectra were recorded as a film on a Perkin Elmer Spectrum One-FT-IR spectrometer fitted with an ATR sampling accessory. Optical rotations were measured in chloroform on a Perkin Elmer 343 Polarimeter; $[\alpha]_D$ values are reported in $10^{-1}$ degrees cm$^2$ g$^{-1}$ at 589 nm. Melting points were recorded using a Reichert hot stage apparatus and are reported uncorrected. HRMS were measured on a Micromass Q-TOPF spectrometer by electrospray ionization (ESI) or electron impact (EI) techniques at the EPSRC Mass Spectrometry Service at the University of Swansea.

### 3.2. $^{19}$F NMR experiment for the observation of the formation of trifluoromethanesulfonic acid formation

A solution of isopropanol (9.1 μL, 0.12 mmol) and 3-(cyclohexylethynyl)-4,4-dimethyloxazolidin-2-one (39.6 mg, 0.18 mmol) in chloroform-$d_1$ (1.2 mL) was added to a sealed reaction vessel containing zinc triflate (3.3 mg, 1.3 μmol) and fluorobenzene (internal standard, 2.8 mg, 0.03 mmol). $^{19}$F NMR experiments were then measured at 20 min intervals over a period of 15 h in order to observe the formation of TfOH. $^{19}$F NMR (376 MHz, chloroform-$d_1$) $\delta$ 37.3 (TfOH), 35.0 ($Zn(OTf)_2$), 0.0 (FPh).

### 3.3. (*E*)-3-(2-Cyclohexyl-1-isopropoxyvinyl)oxazolidin-2-one, *int*-1b

A solution of isopropanol (9.6 μL, 0.13 mmol) and 3-(cyclohexylethynyl)-4,4-dimethyloxazolidin-2-one (41.7 mg, 0.19 mmol) in 1,2-dichloromethane (1.3 mL) was added to a sealed reaction vessel containing zinc triflate (3.5 mg, 1.3 μmol). The solution was stirred under a positive pressure of nitrogen for 24 h at room temperature. Upon completion, the reaction mixture was filtered through a pad of silica, washed with dichloromethane and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography (50% diethyl ether in hexanes) to afford the *enol int*-**1b** (29 mg, 82%) as a colourless oil. $R_f$ 0.37 (50% diethyl ether in hexanes); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 4.68 (d, 1H, $J$=10.3 Hz, C=C*H*Cy), 4.13 (q, 1H, $J$=6.1 Hz, OC*H*(Me)$_2$), 4.04 (s, 2H, OC$H_2$), 1.90–1.87 (m, 1H, *Cy*), 1.69–1.60 (m, 10H, *Cy*), 1.36 (s, 6H, NC$Me_2$), 1.23 (d, 6H, $J$=6.1 Hz, OCH(*Me*)$_2$); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 155.7, 139.1, 114.0, 75.8, 69.5, 59.1, 36.6, 33.0, 27.5, 26.2, 25.9, 21.9; $\nu_{max}$ (film)/cm$^{-1}$ 2923, 1757, 1671, 1449, 1372, 1181, 1043; HRMS (ES$^+$) mass calcd for $C_{16}H_{27}NO_3$ [(M+H)$^+$]: 282.2064; found: 282.2065.

### 3.4. General procedure A: *anti*-aldol reactions

Scandium triflate (5 mol%) and sodium triflate (if stated, 1.0 equiv) were added to the reaction vessel with magnetic stirrer and were dried using a heat gun (>230 °C) for 1 min under high vacuum. After back-filling with nitrogen, ynamide (2.0 equiv) and silanol (2.0 equiv) were added and reaction vessel was sealed with a septum. The reaction vessel was evacuated and back-filled with nitrogen three more times before freshly distilled 1,2-dichloroethane (0.1 M w.r.t. aldehyde) and freshly distilled aldehyde (1.0 equiv) were added. The reaction mixture was stirred at 50 °C for 24–48 h. Once completed, as shown by TLC analysis, the reaction mixture was filtered through a pad of silica, eluted with EtOAc. The solvent was removed under reduced pressure and diastereomeric ratio was obtained by $^1$H NMR spectroscopy of the crude mixture. Product was purified by flash column chromatography on silica gel to afford the aldol product.

*3.4.1. rac-3-((2RS,3SR)-2,3-Diphenyl-3-(triphenylsilyloxy)propanoyl)-4,4-dimethyloxazolidin-2-one,* ***4a****.* General procedure A performed on a 0.25 mmol scale. The crude product (67:33 *anti*/*syn* as determined by $^1$H NMR analysis) was purified by column chromatography (1:4 $Et_2O$/hexanes) to afford **4a** (113 mg, 80%) as a pale yellow solid (Recrystallization by dissolving in a minimum amount of dichloromethane with slow addition of hexane at 0 °C afforded *anti*-**4a** as a white solid.). $R_f$=0.20 (1:4 $Et_2O$/hexane); mp 160 °C; $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.48 (m, 6H, Ar*H*), 7.41–7.35 (m, 3H, Ar*H*), 7.33–7.26 (m, 6H, Ar*H*), 7.13–7.08 (m, 2H, Ar*H*), 7.08–7.03 (m, 3H, Ar*H*), 7.01–6.97 (m, 1H, Ar*H*), 6.96–6.86 (m, 4H, Ar*H*), 5.75 (d, 1H, $J$=9.9 Hz, ($Ph_3SiO$)C*H*), 5.51 (d, 1H, $J$=9.9 Hz, PhC*H*), 3.85 (s, 2H, OC$H_2$), 1.40 (s, 3H, NC*Me*Me′), 1.32 (s, 3H, NCMe*Me*′); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.9, 140.8, 136.1, 135.2, 134.8, 130.0, 129.9, 128.4, 128.2, 127.9, 127.9, 127.8, 127.5, 79.7, 75.2, 61.0, 58.9, 25.2, 24.9; $\nu_{max}$ (film)/cm$^{-1}$ 1772, 1701, 1370, 1304, 1174, 1116, 1087, 909, 737, 710; HRMS (ES$^+$) calcd for $C_{38}H_{35}NO_4Si$ [M+NH$_4$]$^+$ 615.2674, found 615.2669.

*3.4.2. rac-3-((2RS,3SR)-2,3-Diphenyl-3-(triisopropylsilyloxy)propanoyl)-4,4-dimethyloxazolidin-2-one,* ***4b****.* General procedure A was performed on a 0.25 mmol scale. The crude product (80:20 *anti*/*syn* as determined by $^1$H NMR analysis) was purified by column chromatography (1:4 $Et_2O$/hexanes) to afford **4b** (80 mg, 65%) as a yellow oil. $R_f$=0.20 (1:4 $Et_2O$/hexane); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.10 (s, 5H, Ar*H*), 7.07(s, 5H, Ar*H*), 5.49 (d, 1H, $J$=9.6 Hz, (*i*-Pr)$_3$SiOC*H*), 5.44 (d, 1H, $J$=9.6 Hz, PhC*H*), 3.98 (d, 1H, $J$=8.3 Hz, OC*H*H′), 3.87 (d, 1H, $J$=8.3 Hz, OCH*H*′), 1.69 (s, 3H, NC*Me*Me′), 1.44 (s, 3H, NCMe*Me*′), 1.03–0.97 (m, 21H, (*i-Pr*)$_3$Si); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 171.6, 151.8, 140.2, 133.2, 127.6, 126.2, 125.8, 125.7, 125.5, 125.2, 76.2, 73.0, 58.8, 57.7, 23.6, 22.5, 16.3, 16.1, 15.9, 10.8; $\nu_{max}$ (film)/cm$^{-1}$1775, 1703, 1455, 1369, 1314, 1304, 1216, 1173, 1088, 1065, 1038, 882, 806, 697, 679; HRMS (ES$^+$) calcd for $C_{29}H_{41}NO_4Si$ [M+H]$^+$ 496.2878, found 496.2871.

*3.4.3. rac-4,4-Dimethyl-3-((2R,3S)-2-methyl-3-phenyl-3-(triphenylsilyloxy)propanoyl)oxazolidin-2-one,* ***4c****.* General procedure A was performed 0.25 mmol scale. The crude product (67:33 *anti*/*syn* as determined by $^1$H NMR analysis) was purified by column chromatography (1:3 $Et_2O$/hexanes) to afford **4c** (72 mg, 54%) as a colourless oil. Diastereomers were inseparable by recrystallization. $R_f$=0.23 (1:3 $Et_2O$/hexane); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.49–7.09 (m, 40H, major+minor Ar*H*), 5.04 (d, 1H, $J$=9.6 Hz, major $Ph_3SiOCH$), 4.95 (d, 1H, $J$=8.3 Hz, minor $Ph_3SiOCH$), 4.50 (m, 1H, major MeC*H*), 4.32 (m, 1H, minor MeC*H*), 3.90 (d, 1H, $J$=8.3 Hz, major OC*H*H′), 3.77–3.73 (m, 2H, major OCH*H*′+minor OC*H*H′), 3.48 (d, 1H, $J$=8.3 Hz, minor OCH*H*′), 1.50 (s, 3H, major NC*Me*Me′), 1.37 (s, 3H, minor NC*Me*Me′), 1.32 (d, 3H, $J$=6.8 Hz, minor CH*Me*), 1.18 (s, 3H, major NCMe*Me*′), 0.84 (s, 3H, minor NCMe*Me*′), 0.80 (d, 3H, $J$=6.8 Hz, CH*Me*); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 177.5, 176.3, 154.5, 142.2, 141.4, 136.0, 134.7, 134.6, 130.3, 130.1, 128.5, 128.4, 128.3, 128.3, 128.1, 127.9, 80.1, 78.9, 75.2, 47.9, 46.9, 25.3, 25.1, 24.7, 23.9, 15.0, 14.9; $\nu_{max}$ (film)/cm$^{-1}$ 1772, 1700, 1429, 1378, 1305, 1217,

1175, 1115, 1105, 1085, 1064, 1028, 882, 766, 738, 709, 699; HRMS ($ES^+$) calcd for $C_{33}H_{33}NO_4Si$ $[M+H]^+$ 536.2257, found 536.2245.

*3.4.4. rac-4,4-Dimethyl-3-((RS)-2-((SR)-phenyl(triphenylsilyloxy) methyl)octanoyl) oxazolidin-2-one,* ***4d****.* General procedure A was performed on a 0.25 mmol scale. The crude product (80:20 *anti*/*syn* as determined by $^1H$ NMR analysis) was purified by column chromatography (1:5 $Et_2O$/hexanes) to afford **4d** (75 mg, 62%) as a white solid (Recrystallization by dissolving in a minimum amount of dichloromethane with slow addition of hexane at 0 °C afforded *anti*-**4d** as a white solid.). $R_f$=0.19 (1:5 $Et_2O$/hexane); mp 100 °C; $^1H$ NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.57–7.49 (m, 1H, Ar*H*), 7.36–7.30 (m, 2H, Ar*H*), 7.28–7.24 (m, 6H, Ar*H*), 7.19–7.14 (m, 6H, Ar*H*), 7.11–7.69 (m, 5H, Ar*H*), 4.89 (d, 1H, *J*=9.6 Hz, PhC*H*), 4.68 (dt, 1H, *J*=10.8, 3.6 Hz, $(C_6H_{13})CH$), 3.79 (d, 1H, *J*=8.4 Hz, OC*H*H′), 3.57 (d, 1H, *J*=8.4 Hz, OCH*H*′), 1.58 (s, 3H, NC*Me*Me′), 1.11–1.06 (m, 3H, $(CH_2)_5CH_3$), 1.02 (s, 3H, NCMe*Me*′), 1.05–0.92 (m, 6H, $(CH_2)_5CH_3$), 0.90–0.80 (m, 1H, $(CH_2)_5CH_3$), 0.72 (t, 3H, *J*=7.1 Hz, $(CH_2)_5CH_3$); $^{13}C$ NMR (100 MHz, chloroform-$d_1$) $\delta$ 177.5, 154.5, 141.7, 135.9, 135.3, 134.6, 130.5, 130.0, 128.4, 128.3, 128.3, 127.9, 80.2, 74.9, 61.0, 51.8, 31.9, 30.1, 29.5, 27.1, 25.4, 24.8, 22.8, 14.3; $\nu_{max}$ (film)/$cm^{-1}$ 1773, 1697, 1429, 1383, 1305, 1173, 1116, 1086, 1071, 710, 698; HRMS ($ES^+$) calcd for $C_{38}H_{43}NO_4Si$ $[M+NH_4]^+$ 623.3300, found 623.3301. X-ray crystallography deposition number: CCDC 679324.

*3.4.5. rac-3-((RS)-2-((SR)-(2,6-Dimethoxyphenyl)(triphenylsilyloxy) methyl)octanoyl)-4,4-dimethyloxazolidin-2-one,* ***4e****.* General procedure A was performed on a 0.30 mmol scale. The crude product (83:17 *anti*/*syn* as determined by $^1H$ NMR analysis) was purified by column chromatography (1:4 $Et_2O$/hexanes) to afford **4e** (131 mg, 66%) as a clear oil (Recrystallization by dissolving in a minimum amount of dichloromethane with slow addition of Hex at 0 °C afforded *anti*-**4e** as a white solid.). $R_f$=0.20 (1:4 $Et_2O$/hexane); mp 106–108 °C; $^1H$ NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.38–7.35 (m, 6H, Ar*H*), 7.26–7.31 (m, 3H, Ar*H*), 7.23–7.19 (m, 6H, Ar*H*), 6.92 (t, 1H, *J*=8.3 Hz, Ar*H*), 6.18 (d, 1H, *J*=8.2 Hz, Ar*H*), 6.10 (d, 1H, *J*=8.3 Hz, Ar*H*), 5.98 (d, 1H, *J*=10.1 Hz, $Ph_3SiOCH$), 5.45 (dt, 1H, *J*=10.5, 3.9 Hz, $(C_6H_{13})CH$), 3.83 (d, 1H, *J*=8.2 Hz, OC*H*H′), 3.59 (m, 4H, OCH*H*′+O*Me*), 3.37 (s, 3H, O*Me*′), 1.50 (s, 3H, NC*Me*Me′), 1.22 (s, 3H, NCMe*Me*′), 1.2–0.9 (m, 10H, $(CH_2)_5CH_3$), 0.84 (t, 3H, *J*=7.1 Hz, $(CH_2)_5CH_3$); $^{13}C$ NMR (100 MHz, chloroform-$d_1$) $\delta$ 178.8, 159.9, 158.1, 154.0, 135.4, 135.1, 129.2, 129.2, 127.2, 116.3, 104.3, 103.1, 74.4, 70.8, 55.4, 55.1, 47.6, 31.6, 29.4, 29.3, 26.8, 25.1, 24.3, 22.5, 14.0; $\nu_{max}$ (film)/$cm^{-1}$ 2931, 1777, 1695, 1594, 1475, 1305, 1115, 1107, 1085, 710, 700; HRMS ($ES^+$) calcd for $C_{40}H_{47}NO_6Si$ $[M+Na]^+$ 688.3070, found 688.3110.

*3.4.6. rac-4,4-Dimethyl-3-((2RS,3RS)-2-phenyl-3-(triphenylsilyloxy) hexanoyl)oxazolidin-2-one,* ***4f****.* General procedure A was performed on a 0.22 mmol scale. The crude product (86:14 *anti*/*syn* as determined by $^1H$ NMR analysis) was purified by column chromatography (1:4 $Et_2O$/hexanes) to afford **4f** (141 mg, 57%) as a white solid (Recrystallization by dissolving in a minimum amount of dichloromethane with slow addition of Hex at 0 °C afforded *anti*-**4f** as a white solid.). $R_f$=0.18 (1:4 $Et_2O$/hexane); mp 106 °C; $^1H$ NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.75–7.71 (m, 6H, Ar*H*), 7.47–7.36 (m, 11H, Ar*H*), 7.31–7.24 (m, 3H, Ar*H*), 5.55 (d, 1H, *J*=9.7 Hz, PhC*H*), 4.83 (dt, 1H, *J*=9.7, 5.1 Hz, $Ph_3SiOCH$), 3.74 (ABq, 2H, *J*=8.3 Hz, $OCH_2$), 1.35–1.30 (m, 2H, $Ph_3SiOCHCH_2$), 1.29 (s, 3H, NC*Me*Me′), 1.24–1.15 (m, 2H, $CH_3CH_2$), 1.07 (s, 3H, NCMe*Me*′), 0.46 (t, 3H, *J*=6.8 Hz, $CH_3CH_2$); $^{13}C$ NMR (100 MHz, chloroform-$d_1$) $\delta$ 174.3, 154.3, 136.5, 136.1, 135.5, 130.2, 129.7, 128.9, 128.1, 127.9, 75.7, 75.1, 60.9, 56.4, 36.3, 25.0, 24.7, 17.3, 14.0; $\nu_{max}$ (film)/$cm^{-1}$ 1769, 1703, 1428, 1317, 1303, 1114, 1104, 1091, 1037, 698; HRMS ($ES^+$) calcd for $C_{35}H_{37}NO_4Si$ $[M+Na]^+$ 586.2384, found 586.2374. X-ray crystallography deposition number: CCDC 679323.

*3.4.7. rac-4,4-Dimethyl-3-((2RS,3RS)-4-methyl-2-phenyl-3-(triphenylsilyloxy)pentanoyl)oxazolidin-2-one,* ***4g****.* General procedure A was performed on a 0.27 mmol scale. The crude product (>95:5 *anti*/*syn* as determined by $^1H$ NMR analysis) was purified by column chromatography (1:4 $Et_2O$/hexanes) to afford **4g** (108 mg, 73%) as a white solid. $R_f$=0.38 (1:2 $Et_2O$/hexane); mp 146 °C; $^1H$ NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.76 (m, 6H, Ar*H*), 7.44–7.38 (m, 9H, Ar*H*), 7.30–7.21 (m, 5H, Ar*H*), 5.62 (d, 1H, *J*=9.7 Hz, PhC*H*), 4.62 (dd, 1H, *J*=9.8, 1.4 Hz, $Ph_3SiOCH$), 3.67 (ABq, 2H, *J*=15.0, 8.2 Hz, $OCH_2$), 1.29 (m, 1H, $CH(Me)_2$), 1.05 (s, 3H, NC*Me*Me′), 0.99 (d, 3H, *J*=6.8 Hz, CH(*Me*)(Me′)), 0.83 (s, 3H, NCMe*Me*′), 0.73 (d, 3H, *J*=6.9 Hz, CH(Me)(*Me*′)); $^{13}C$ NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.9, 154.1, 136.5, 136.1, 135.9, 130.5, 129.6, 128.9, 127.8, 127.7, 78.9, 75.0, 60.7, 56.0, 30.4, 30.1, 24.8, 24.2, 20.9, 15.0; $\nu_{max}$ (film)/$cm^{-1}$ 1771, 1702, 1429, 1375, 1305, 1177, 1114, 1088, 1051, 909, 735; HRMS ($ES^+$) calcd for $C_{35}H_{38}NO_4Si$ $[M+H]^+$ 564.2570, found 564.2584.

*3.4.8. rac-3-((2RS,3RS)-3-Cyclohexyl-2-phenyl-3-(triphenylsilyloxy) propanoyl)-4,4-dimethyloxazolidin-2-one,* ***4h****.* General procedure A was performed on a 0.41 mmol scale. The crude product (>95:5 *anti*/*syn* as determined by $^1H$ NMR analysis) was purified by column chromatography (1:3 $Et_2O$/hexanes) to afford **4h** (178 mg, 72%) as a white amorphous solid. $R_f$=0.21 (1:3 $Et_2O$/hexane); $^1H$ NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.72 (m, 6H, Ar*H*), 7.44–7.33 (m, 9H, Ar*H*), 7.28–7.18 (m, 5H, Ar*H*), 5.65 (d, 1H, *J*=9.8 Hz, PhC*H*), 4.56 (appt. d, 1H, *J*=9.8 Hz, $Ph_3SiOCH$), 3.63 (ABq, 2H, *J*=10.7, 8.4 Hz, $OCH_2$), 1.74–1.61 (m, 2H, Cy*H*), 1.52–1.28 (m, 5H, Cy*H*), 1.12–1.06 (m, 1H, Cy*H*), 1.03 (s, 3H, NC*Me*Me′), 0.99–0.85 (m, 2H, Cy*H*), 0.82 (s, 3H, NCMe*Me*′), 0.85–0.75 (m, 1H, Cy*H*); $^{13}C$ NMR (100 MHz, chloroform-$d_1$) $\delta$ 174.1, 145.1, 136.5, 136.2, 136.0, 135.4, 130.0, 129.6, 128.9, 128.3, 127.9, 127.8, 79.1, 75.0, 60.7, 55.1, 40.9, 30.5, 26.8, 26.8, 26.6, 25.8, 24.9, 24.3; $\nu_{max}$ (film)/$cm^{-1}$ 1773, 1702, 1429, 1377, 1315, 1303, 1175, 1113, 1086, 908, 734, 708, 700; HRMS ($ES^+$) calcd for $C_{38}H_{41}NO_4Si$ $[M+Na]^+$ 626.2703, found 626.2707.

*3.4.9. rac-3-((2RS,3RS,4SR)-2,4-Diphenyl-3-(triphenylsilyloxy)pentanoyl)-4,4-dimethyloxazolidin-2-one,* ***4i****.* General procedure A was performed on a 0.37 mmol scale. The crude product (>95:5 *antisyn* as determined by $^1H$ NMR analysis, a 3:1 Felkin to *anti*-Felkin product) was purified by column chromatography (1:4 EtOAc/hexanes) to afford **4i** (99 mg, 43%) as a white amorphous solid (Recrystallization by dissolving in a minimum amount of dichloromethane with slow addition of Hex at 0 °C afforded *anti*-**4i** Felkin product as a white solid.). $R_f$=0.29 (1:4 EtOAc/hexane); mp 215–216 °C; $^1H$ NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.39–7.23 (m, 20H, ArH), 7.07 (t, 1H, *J*=7.3 Hz, Ar*H*), 6.50 (t, 2H, *J*=7.8 Hz, Ar*H*), 6.78 (d, 2H, *J*=7.3 Hz, Ar*H*), 5.72 (d, 1H, *J*=9.7 Hz, PhC*H*), 4.80 (dd, 1H, *J*=9.7, 1.3 Hz, $Ph_3SiOCH$), 3.67 (ABq, 2H, *J*=8.2, 12.1 Hz, $OCH_2$), 2.44 (q, 1H, *J*=6.97 Hz, MeC*H*), 1.43 (d, 3H, *J*=7.0 Hz, *Me*CH), 1.02 (s, 3H, NC*Me*Me′), 0.77 (s, 3H, NCMe*Me*′); $^{13}C$ NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.3, 154.1, 144.7, 136.6, 135.8, 135.6, 129.7, 129.4, 129.2, 128.8, 128.1, 127.8, 126.1, 79.9, 75.0, 60.7, 56.6, 40.5, 24.7, 24.3, 11.3; $\nu_{max}$ (film)/$cm^{-1}$ 1771, 1702, 1312, 1115, 1088, 908, 732, 698; HRMS ($ES^+$) calcd for $C_{40}H_{39}NO_4Si$ $[M+NH_4]^+$ 643.2987, found 643.2984. X-ray crystallography deposition number: 679325.

*3.4.10. (S)-4-tert-Butyl-3-((2R,3R)-4-methyl-2-phenyl-3-(triphenylsilyloxy)pentanoyl)oxazolidin-2-one,* ***4j****.* General procedure A was performed on a 0.17 mmol scale. The crude product (94:6 *anti*/*syn* as determined by $^1H$ NMR analysis) was purified by column chromatography (1:4 $Et_2O$/hexanes) to afford **4j** (44 mg, 44%) as a colourless oil. $R_f$=0.22 (1:4 $Et_2O$/hexane); $^1H$ NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.73–7.72 (m, 6H, Ar*H*), 7.41–7.35 (m, 11H, Ar*H*),

7.25–7.19 (m, 3H, Ar*H*), 5.63 (d, 1H, *J*=10.0 Hz, PhC*H*), 4.73 (dd, 1H, *J*=10.0, 1.2 Hz, $Ph_3SiOCH$), 3.94 (dd, 1H, *J*=8.8, 1.6 Hz, NC*H*), 3.75 (t, 1H, *J*=8.8 Hz, OC*H*H′), 3.62 (dd, 1H, *J*=8.0, 1.6 Hz, OCH*H*′), 1.34 (m, 1H, C*H*(Me)(Me′)), 0.96 (d, 3H, *J*=6.8 Hz, CH(*Me*)(Me′)), 0.63 (d, 3H, *J*=6.8 Hz, CH(Me)(*Me*′)), 0.48 (s, 9H, *t-Bu*); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 172.8, 154.3, 136.1, 135.8, 135.5, 129.5, 128.4, 127.5, 78.3, 77.2, 64.5, 60.0, 53.9, 35.8, 29.7, 25.1, 20.4, 14.9, 14.6 (2 aromatic carbon signals missing due to overlap); $\nu_{max}$ (film)/cm$^{-1}$ 2965, 1775, 1705, 1182, 1105, 1114, 1050, 710, 700; $[\alpha]_D^{25}$ +6.0 (*c* 0.1, $CHCl_3$); HRMS (ES$^+$) calcd for $C_{37}H_{41}NO_4Si$ $[M+NH_4]^+$ 609.3143, found 609.3136.

*3.4.11. (3S)-3-tert-Butyl-2-((2R,3R)-3-hydroxy-4-methyl-2-phenylpentanoyl)cyclopentanone,* ***4k****.* General procedure A was performed on a 0.20 mmol scale. The crude product (>95:5 *anti*/*sum of all others* as determined by $^1$H NMR analysis) was purified by column chromatography (1:4 EtOAc/hexanes grading to 1:2 EtOAc/hexanes) to afford **4k** (35 mg, 52%) as a white solid. $R_f$=0.10 (1:4 EtOAc/hexane); mp 106 °C; $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.39 (m, 2H, Ph*H*), 7.26–7.17 (m, 3H, Ph*H*), 5.23 (d, 1H, *J*=9.6 Hz, PhC*H*), 4.42 (dd, 1H, *J*=6.8, 2.9 Hz, NC*H*), 4.21–4.14 (m, 3H, O$CH_2$+HOC*H*), 2.21 (d, 1H, *J*=6H, O*H*), 1.41 (m, 1H, C*H*(Me)(Me′)), 0.85 (d, 3H, *J*=7.2 Hz, CH(*Me*)(Me′)), 0.81 (d, 3H, *J*=6.8 Hz, CH(Me)(*Me*′)), 0.62 (s, 9H, *t-Bu*); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 174.3, 154.7, 136.1, 129.7, 129.0, 128.1, 65.5, 61.1, 53.5, 36.4, 29.2, 25.7, 20.8, 14.6; $\nu_{max}$ (film)/cm$^{-1}$ 3600–3300 (br), 2963, 1778, 1702, 1370, 1186, 723; $[\alpha]_D^{25}$ +18 (*c* 0.27, $CHCl_3$); HRMS (ES$^+$) calcd for $C_{19}H_{27}NO_4$ $[M+H]^+$ 334.2013, found 334.2013. X-ray crystallography deposition number: CCDC 679326.

*3.4.12. (S)-4-tert-Butyl-3-((2R,3R)-3-cyclohexyl-3-hydroxy-2-phenylpropanoyl)oxazolidin-2-one,* ***4l****.* General procedure A was performed on a 0.20 mmol scale. The crude product (>95:5 *anti*/*sum of all others* as determined by $^1$H NMR analysis) was purified by column chromatography (1:4 EtOAc/hexanes grading to 1:2 EtOAc/hexanes) to afford **4l** (37 mg, 50%) as a colourless oil. $R_f$=0.15 (1:4 EtOAc/hexane); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.45–7.44 (m, 2H, Ph*H*), 7.32–7.24 (m, 3H, Ph*H*), 5.34 (d, 1H, *J*=9.5 Hz, PhC*H*), 4.48 (dd, 1H, *J*=7.1, 2.3 Hz, NC*H*), 4.25–4.16 (m, 3H, O$CH_2$+HOC*H*), 2.32 (br s, 1H, O*H*), 1.76–1.06 (br m, 11H, Cy*H*), 0.68 (s, 9H, *t*-Bu); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 174.0, 157.2, 135.7, 129.3, 128.6, 127.6, 65.1, 60.7, 52.2, 38.9, 36.0, 30.6, 26.4, 26.3, 26.0, 25.3, 25.0, 24.8; $\nu_{max}$ (film)/cm$^{-1}$ 3502, 2927, 1779, 1701, 1369, 1220, 1184, 1111, 724; $[\alpha]_D^{25}$ +0.6 (*c* 0.57, $CHCl_3$); HRMS (ES$^+$) calcd for $C_{22}H_{31}NO_4$ $[M+Na]^+$ 396.2151, found 396.2165.

*3.4.13. (S)-4-tert-Butyl-3-((2R,3R)-3-hydroxy-2-phenylhexanoyl)oxazolidin-2-one,* ***4m****.* General procedure A was performed on a 0.20 mmol scale. The crude product (>95:5 *anti*/*sum of all others* as determined by $^1$H NMR analysis) was purified by column chromatography (1:4 EtOAc/hexanes grading to 1:2 EtOAc/hexanes) to afford **4m** (33 mg, 50%) as a colourless oil. $R_f$=0.10 (1:4 EtOAc/hexane); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.44–7.42 (m, 2H, Ph*H*), 7.32–7.25 (m, 3H, Ph*H*), 5.07 (d, 1H, *J*=9.5 Hz, PhC*H*), 4.49 (dd, 1H, *J*=7.2, 2.2 Hz, NC*H*), 4.28 (m, 1H, HOC*H*), 4.22 (m, 2H, O$CH_2$), 1.25 (m, 4H, $CH_3CH_2CH_2$), 0.82 (t, 3H, *J*=7.0 Hz, $CH_3$), 0.68 (s, 9H, *t-Bu*); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.7, 154.1, 135.7, 129.3, 128.6, 127.7, 73.2, 65.1, 60.7, 56.0, 36.0, 35.8, 25.3, 18.5, 13.8; $\nu_{max}$ (film)/cm$^{-1}$ 3470, 2961, 2872, 1779, 1702,1370, 1121, 1188, 1117, 723, 700; $[\alpha]_D^{25}$ +4.9 (*c* 0.57, $CHCl_3$); HRMS (ES$^+$) calcd for $C_{19}H_{27}NO_4$ $[M+Na]^+$ 356.1838, found 356.1846.

*3.4.14. (S)-4-tert-Butyl-3-((2R,3R)-3-hydroxy-2-phenylhexanoyl)oxazolidin-2-one,* ***4n****.* General procedure A was performed on a 0.20 mmol scale. The crude product (>95:5 *anti*/*sum of all others* as determined by $^1$H NMR analysis) was purified by column chromatography (1:4 EtOAc/hexanes grading to 1:2 EtOAc/hexanes) to afford **4n** (48 mg, 61%) as a colourless oil. $R_f$=0.10 (1:4 EtOAc/hexane); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.40–7.36 (m, 2H, Ar*H*), 7.32–7.18 (m, 5H, Ar*H*), 7.15–7.12 (m, 1H, Ar*H*), 7.06–7.03 (m, 2H, Ar*H*), 5.11 (d, 1H, *J*=9.5 Hz, PhC*H*), 4.47 (dd, 1H, *J*=7.0, 2.3 Hz, NC*H*), 4.32 (br m, 1H, OHC*H*), 4.26–4.19 (m, 2H, $OCH_2$), 2.82 (m, 1H, PhC*H*H′), 2.58 (m, 1H, PhCH*H*′), 2.50 (br s, 1H, OH), 1.63 (m, 2H, $PhCH_2CH_2$), 0.68 (s, 9H, *t-Bu*); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.6, 154.0, 141.7, 135.4, 129.3, 128.6, 128.4, 128.3, 127.8, 125.7, 72.8, 65.1, 60.7, 56.0, 36.0, 35.2, 31.6, 25.3; $\nu_{max}$ (film)/cm$^{-1}$ 3459, 2963, 1778, 1702, 1370; $[\alpha]_D^{25}$ −7.5 (*c* 0.36, $CHCl_3$); HRMS (ES$^+$) calcd for $C_{24}H_{29}NO_4$ $[M+Na]^+$ 418.1994, found 418.1992.

### 3.5. General procedure B: Ficini–Claisen rearrangement

Metal triflate and additive were added to a reaction vessel, which was sealed under a positive pressure of nitrogen with magnetic stirring. Allyl alcohol (1.0 equiv) and ynamide (1.5 equiv) were azeotroped with toluene (3×25 mL), and dried in vacuo, before being dissolved in 1,2-dichloroethane (0.1 M with respect to the allyl alcohol) and added to the reaction vessel. The reaction mixture was stirred at room temperature for 24 h, unless stated otherwise. Once complete, the reaction mixture was filtered through a pad of silica and washed with dichloromethane. The reaction mixture was evaporated to dryness under reduced pressure and the residue purified by column chromatography.

*3.5.1. rac-(2RS,3SR)-3-(2,3-Diphenyl-pent-4-enoyl)-4,4-dimethyloxazolidin-2-one,* ***6a****.* General procedure B performed on a 0.13 mmol scale. The crude product (>95:5 *syn*/*anti* as determined by $^1$H NMR analysis) was purified by column chromatography (50% diethyl ether in hexanes) to afford the *amide* **6a** (38 mg, 88%) as a white solid. $R_f$ 0.46 (50% diethyl ether in hexanes); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.21–7.19 (m, 2H, Ph*H*), 7.12–7.06 (m, 5H, Ph*H*), 7.05–7.00 (m, 3H, Ph*H*), 6.13 (ddd, 1H, *J*=17.4, 11.0, 8.0 Hz, $CH_2$=C*H*), 5.56 (d, 1H, *J*=11.3 Hz, C(O)C*H*), 5.20 (dd, 1H, *J*=17.2, 1.1 Hz, CH=C$H^{cis}$H$^{trans}$), 5.10 (dt, 1H, *J*=10.3, 0.7 Hz, CH=CH$^{cis}$$H^{trans}$), 4.14 (dd, 1H, *J*=12.4, 8.1 Hz, $CH_2$=CHC*H*), 3.97 (d, 1H, *J*=8.4 Hz, OC*H*H′), 3.87 (d, 1H, *J*=8.4 Hz, OCH*H*′), 1.59 (s, 3H, NC*Me*Me′), 1.41 (s, 3H, NCMe*Me*′); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.4, 153.9, 140.6, 139.8, 136.5, 129.3, 128.5, 128.1, 128.1, 127.0, 115.8, 74.9, 60.8, 53.9, 53.8, 30.9, 25.0, 24.5; $\nu_{max}$ (film)/cm$^{-1}$ 2972, 1772, 1701, 1320, 1271; HRMS (ES$^+$) mass calcd for $C_{22}H_{23}NO_3$ [(M+H)$^+$]: 350.1756; found: 350.1751.

*3.5.2. rac-(2RS,3SR)-4,4-Dimethyl-3-[2-(1-phenylallyl)-octanyl]-oxazolidin-2-one,* ***6b****.* General procedure B performed on a 0.21 mmol scale. The crude product (90:10 *syn*/*anti* as determined by $^1$H NMR analysis) was purified by column chromatography (20% diethyl ether in hexanes) to afford *amide* **6b** (71 mg, 97%) as a colourless oil. $R_f$ 0.66 (50% diethyl ether in hexanes); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.31–7.18 (m, 5H, Ph*H*), 6.01 (ddd, 1H, *J*=17.0, 9.7, 7.3 Hz, $CH_2$=C*H*), 5.03 (dd, 1H, *J*=17.0, 1.6 Hz, CH=C$H^{trans}$H$^{cis}$), 4.94 (dd, 1H, *J*=10.1, 1.7 Hz, CH=CH$^{trans}$$H^{cis}$), 4.44 (td, 1H, *J*=10.5, 3.5 Hz, C(O)C*H*), 3.98 (AB q, 2H, *J*=8.4 Hz, O$CH_2$), 3.44 (t, 1H, *J*=10.0 Hz, PhC*H*), 1.58 (s, 3H, NC*Me*Me′), 1.53 (s, 3H, NCMe*Me*′), 1.25–1.12 (m, 10H, $(CH_2)_5CH_3$), 0.81 (t, 3H, *J*=7.2 Hz, $(CH_2)_5CH_3$); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 177.1, 154.2, 141.9, 139.7, 128.6, 128.0, 126.6, 115.7, 74.8, 60.9, 55.1, 47.8, 31.5, 31.4, 29.1, 27.1, 25.0, 24.7, 22.4, 13.9; $\nu_{max}$ (film)/cm$^{-1}$ 2926, 1770, 1698, 1377, 1172, 1086; HRMS (ES$^+$) mass calcd for $C_{22}H_{31}NO_3$ [(M+H)$^+$]: 358.2377; found: 358.2377.

*3.5.3. rac-(2RS,3RS)-4,4-Dimethyl-3-(3-phenyl-2-thiophen-3-yl-pent-4-enoyl)-oxazolidin-2-one,* ***6c****.* General procedure B performed on a 0.6 mmol scale. The crude product (>95:5 *syn*/*anti* as determined by $^1$H NMR analysis) was purified by column chromatography (40%

diethyl ether in hexanes) to afford *amide* **6c** (160 mg, 78%) as a white solid. $R_f$ 0.56 (50% diethyl ether in hexanes); mp 68–70 °C; $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.16–7.02 (m, 6H, Ar*H*), 6.97 (dd, 1H, *J*=3.1, 1.4 Hz, Ar*H*), 6.88 (dd, 1H, *J*=4.9, 1.4 Hz, Ar*H*), 6.10 (ddd, 1H, *J*=17.8, 10.3, 8.0 Hz, $CH_2$=C*H*), 5.67 (d, 1H, *J*=11.2 Hz, C(O)C*H*), 5.18 (dt, 1H, *J*=17.8, 1.2 Hz, CH=C*H*$^{trans}$H$^{cis}$), 5.09 (dq, 1H, *J*=10.4, 1.2 Hz, CH=CH$^{trans}$*H*$^{cis}$), 4.08 (app q, 1H, *J*=8.0 Hz, PhC*H*), 3.99 (d, 1H, *J*=8.4 Hz, OC*H*H′), 3.91 (d, 1H, *J*=8.4 Hz, OCH*H*′), 1.59 (s, 3H, NC*Me*Me′), 1.46 (s, 3H, NCMe*Me*′); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.7, 153.9, 140.7, 139.5, 136.8, 128.5, 128.2, 127.8, 126.4, 124.2, 123.5, 116.0, 74.9, 60.8, 54.1, 49.8, 24.9, 24.5; $\nu_{max}$ (film)/cm$^{-1}$ 2929, 1771, 1702, 1305, 1176, 1091; HRMS (ES$^+$) mass calcd for $C_{20}H_{21}NO_3S$ [(M+H)$^+$]: 356.1320; found: 356.1323.

*3.5.4. rac-(2SR,3RS)-3-(2-Cyclohexyl-3-phenyl-pent-4-enoyl)-4,4-dimethyloxazolidin-2-one,* ***6d****.* General procedure B performed on a 0.26 mmol scale. The crude product (>95:5 *syn:anti* as determined by $^1$H NMR analysis) was purified by column chromatography (30% diethyl ether in hexanes) to afford *amide* **6d** (70 mg, 66%) as a colourless oil. $R_f$ 0.33 (50% diethyl ether in hexanes); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.30–7.24 (m, 3H, Ph*H*), 7.20–7.17 (m, 2H, Ph*H*), 6.14 (ddd, 1H, *J*=17.1, 10.1, 1.4 Hz, $CH_2$=C*H*), 5.07 (dd, 1H, *J*=17.1, 1.7 Hz, CH=C*H*$^{trans}$H$^{cis}$), 5.03 (dd, 1H, *J*=10.1, 1.7 Hz, CH=CH$^{trans}$*H*$^{cis}$), 4.53 (dd, 1H, *J*=9.4, 6.3 Hz, C(O)C*H*), 3.88 (d, 1H, *J*=8.4 Hz, OC*H*H′), 3.80–3.74 (m, 2H, OCH*H*′+PhC*H*), 1.79–1.60 (m, 3H, *c*-Hex*H*), 1.56 (s, 3H, NC*Me*Me′), 1.40 (s, 3H, NCMe*Me*′), 1.25–0.83 (m, 8H, *c*-Hex*H*); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 175.8, 142.0, 139.1, 128.5, 128.0, 126.4, 116.2, 74.5, 60.9, 51.6, 50.4, 38.9, 31.0, 28.9, 26.5, 26.4, 24.9, 24.5; $\nu_{max}$ (film)/cm$^{-1}$ 2928, 2853, 1767, 1694, 1305, 1172, 1089; HRMS (ES$^+$) mass calcd for $C_{22}H_{29}NO_3$ [(M+H)$^+$]: 356.2226; found: 356.2228.

*3.5.5. (2R,3R)-4,4-Dimethyl-3-[2-phenyl-3-(4-trifluoromethyl-phenyl)-pent-4-enoyl]-oxazolidin-2-one,* ***6e****.* General procedure B performed on a 0.12 mmol scale. The crude product (>95:5 *syn*/*anti* as determined by $^1$H NMR analysis) was purified by column chromatography (20% diethyl ether in hexanes) to afford the *amide* **6e** (39 mg, 76%) as a white solid. $R_f$ 0.42 (50% diethyl ether in hexanes); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.35 (d, 2H, *J*=8.1 Hz, Ar*H*), 7.21–7.16 (m, 2H, Ar*H*), 7.16–7.07 (m, 5H, Ar*H*), 6.09 (ddd, 1H, *J*=17.5, 11.0, 7.7 Hz, $CH_2$=C*H*), 5.57 (d, 1H, *J*=11.0 Hz, C(O)C*H*), 5.23 (dd, 1H, *J*=17.2, 1.5 Hz, CH=C*H*$^{trans}$H$^{cis}$), 5.15 (dd, 1H, *J*=11.0, 1.5 Hz, CH=CH$^{trans}$*H*$^{cis}$), 4.25 (dd, 1H, *J*=11.1, 7.7 Hz, $CH_2$=CHC*H*), 3.99 (d, 1H, *J*=8.4 Hz, OC*H*H′), 3.89 (d, 1H, *J*=8.4 Hz, OCH*H*′), 1.57 (s, 3H, NC*Me*Me′), 1.41 (s, 3H, NCMe*Me*′); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.9, 154.2, 146.3, 136.4, 133.1, 130.8, 129.6 (q, *J*=32.5 Hz), 129.2, 128.2, 127.4, 125.3 (q, *J*=3.9 Hz), 123.4 (q, *J*=275.0 Hz), 121.7, 61.2, 54.3, 54.2, 25.3, 24.8; $\nu_{max}$ (film)/cm$^{-1}$ 2871, 1782, 1698, 1302, 1173; HRMS (ES$^+$) mass calcd for $C_{23}H_{22}F_3NO_3$ [(M+H)$^+$]: 418.1630; found: 418.1632.

*3.5.6. rac-(2RS,3SR)-(E)-4,4-Dimethyl-3-(2-phenyl-3-vinylhex-4-enoyl)-oxazolidin-2-one,* ***6f****.* General procedure B performed on a 0.16 mmol scale. The crude product (>95:5 *syn:anti* as determined by $^1$H NMR analysis) was purified by column chromatography (20% diethyl ether in hexanes) to afford the *amide* **6f** (28 mg, 59%) as a colourless oil. $R_f$ 0.65 (50% diethyl ether in hexanes); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.37–7.34 (m, 1H, Ph*H*), 7.30–7.28 (m, 2H, Ph*H*), 7.24–7.22 (m, 2H, Ph*H*), 5.85 (ddd, 1H, *J*=17.8, 10.3, 7.9 Hz, $CH_2$=C*H*), 5.26–5.19 (m, 1H, MeHC=C*H*), 5.14–5.04 (m, 4H, C*H*$_2$=CH +Me*H*C=CH+C(O)C*H*), 3.93 (d, 1H, *J*=8.4 Hz, OC*H*H′), 3.86 (d, 1H, *J*=8.4H, OCH*H*′), 3.53 (br q, 1H, *J*=8.8 Hz, PhCHC*H*), 1.55 (s, 3H, NC*Me*Me′), 1.44 (dm, 3H, *J*=7.6 Hz, *Me*HC=C), 1.39 (s, 3H, NCMe*Me*′); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 174.0, 153.8, 139.2, 137.0, 130.1, 129.5, 128.3, 127.4, 127.2, 115.8, 74.9, 60.8, 53.5, 50.4, 24.9, 24.5, 18.0; $\nu_{max}$ (film)/cm$^{-1}$ 2924, 1776, 1700, 1300, 1173; HRMS (ES$^+$) mass calcd for $C_{19}H_{23}NO_3$ [(M+H)$^+$]: 314.1756; found: 314.1757.

*3.5.7. rac-(2RS,3RS)-4,4-Dimethyl-3-(2-phenyl-3-ethyl-pent-4-enoyl)-oxazolidinone,* ***6g****.* General procedure B performed on a 0.5 mmol scale. The crude product (>95:5 *syn*/*anti* as determined by $^1$H NMR analysis) was purified by column chromatography (20% diethyl ether in hexanes) to afford *amide* **6g** (25 mg, 54%) as a colourless oil. $R_f$ 0.51 (50% diethyl ether in hexanes); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.43–7.41 (m, 2H, Ph*H*), 7.33–7.25 (m, 3H, Ph*H*), 5.67 (ddd, 1H, *J*=17.3, 9.4, 8.8 Hz, $CH_2$=C*H*), 5.11 (dd, 1H, *J*=17.4, 1.8 Hz, CH=C*H*$^{trans}$H$^{cis}$), 5.09 (dd, 1H, *J*=9.5, 1.8 Hz, CH=CH$^{trans}$*H*$^{cis}$), 5.02 (d, 1H, *J*=10.6 Hz, PhC*H*), 3.92 (d, 1H, *J*=8.3 Hz, OC*H*H′), 3.85 (d, 1H, *J*=8.3 Hz, OCH*H*′), 2.77 (ddt, 1H, *J*=10.5, 9.5, 3.3 Hz, $CH_2$=CHC*H*), 1.53 (s, 3H, NC*Me*Me′), 1.37 (s, 3H, NCMe*Me*′), 1.20–1.14 (m, 1H, CH*H*′CH$_3$), 1.06–0.98 (m, 1H, C*H*H′CH$_3$), 0.74 (t, 3H, *J*=7.51 Hz, $CH_2$C*H*$_3$); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 174.4, 153.9, 139.9, 137.2, 129.4, 128.4, 127.3, 117.1, 76.7, 74.8, 60.8, 53.5, 49.2, 24.9, 24.5, 11.2; $\nu_{max}$ (film)/cm$^{-1}$ 2968, 1786, 1700, 1403, 1302, 1173; HRMS (ES$^+$) mass calcd for $C_{18}H_{23}NO_3$ [(M+H)$^+$]: 302.1751; found: 302.1749.

*3.5.8. rac-(2RS,3RS)-(E)-4,4-Dimethyl-3-(3-methyl-2-phenylhex-4-enoyl)-oxazolidin-2-one, (±)-****6h****.* General procedure B performed on a 0.5 mmol scale. The crude product (>95:5 *syn*/*anti* as determined by $^1$H NMR analysis) was purified by column chromatography (30% diethyl ether in hexanes) to afford *amide* (±)-**6h** (100 mg, 63%) as a white solid. $R_f$ 0.61 (50% diethyl ether in hexanes); mp 63–65 °C; $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.43–7.40 (m, 2H, Ph*H*), 7.31–7.21 (m, 3H, Ph*H*), 5.54 (ddq, 1H, *J*=17.2, 8.0, 6.3 Hz, MeHC=C*H*), 5.40 (dq, 1H, *J*=17.1, 1.4 Hz, Me*H*C=CH), 4.84 (d, 1H, *J*=10.8 Hz, PhC*H*), 3.92 (d, 1H, *J*=8.4 Hz, OC*H*H′), 3.85 (d, 1H, *J*=8.3 Hz, OCH*H*′), 2.93 (ddq, 1H, *J*=10.8, 8.0, 6.2 Hz, MeHC=CHC*H*), 1.64 (dd, 3H, *J*=6.3, 1.4 Hz, *Me*HC=C), 1.52 (s, 3H, NC*Me*Me′), 1.40 (s, 3H, NCMe*Me*′), 0.74 (d, 3H, *J*=6.2 Hz, *Me*CH); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 174.6, 153.9, 137.5, 135.5, 129.3, 128.4, 127.2, 125.6, 74.8, 60.6, 55.4, 41.2, 24.6, 18.5, 17.9; $\nu_{max}$ (film)/cm$^{-1}$ 2967, 2926, 1772, 1701, 1200, 1174, 1087; HRMS (ES$^+$) mass calcd for $C_{18}H_{23}NO_3$ [(M+H)$^+$]: 302.1751; found: 302.1753.

*3.5.9. (2S,3S)-(E)-4,4-Dimethyl-3-[2-phenyl-3-(4-trifluoromethyl-phenyl)-hex-4-enoyl]-oxazolidin-2-one, (+)-****6i****.* General procedure B performed on a 0.16 mmol scale. The crude product (>95:5 *syn*/*anti* as determined by $^1$H NMR analysis) was purified by column chromatography (30% diethyl ether in hexanes) to afford the *amide* (+)-**6i** (41 mg, 60%) as a colourless oil. $R_f$ 0.54 (50% diethyl ether in hexanes); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.34 (d, 2H, *J*=8.4 Hz, Ar*H*), 7.22–7.18 (m, 2H, Ar*H*), 7.14–7.08 (m, 5H, Ar*H*), 5.68 (dd, 1H, *J*=17.1, 7.3 Hz, MeHC=C*H*), 5.64 (dq, 1H, *J*=17.1, 5.9 Hz, Me*H*C=CH), 5.55 (d, 1H, *J*=11.1 Hz, PhC*H*), 4.14 (dd, 1H, *J*=11.1, 7.3 Hz, MeHC=CHC*H*), 3.97 (d, 1H, *J*=8.4 Hz, OC*H*H′), 3.89 (d, 1H, *J*=8.4 Hz, OCH*H*′), 1.66 (d, 3H, *J*=5.9 Hz, *Me*CH=CH), 1.57 (s, 3H, NC*Me*Me′), 1.43 (s, 3H, NCMe*Me*′); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.7, 153.9, 145.9, 136.1, 131.6, 129.2, 128.6, 128.4 (q, *J*=32.3 Hz), 128.2, 127.2, 125.0 (q, *J*=3.8 Hz), 123.7 (q, *J*=272.0 Hz), 122.8, 74.9, 60.8, 53.1, 52.1, 24.9, 24.5, 18.0; $\nu_{max}$ (film)/cm$^{-1}$ 2964, 2923, 1782, 1303, 1201, 1174, 1087; $[\alpha]_D^{25}$ +37.6 (*c* 0.019, $CHCl_3$); HRMS (ES$^+$) mass calcd for $C_{24}H_{24}F_3NO_3$ [(M+H)$^+$]: 432.1787; found: 432.1807.

Chiral separation: column: Chiralpak AD-H; flow rate: 0.5 mL/min; solvent: 99% hexane/IPA; retention times: enantiomer 1: 25.74 min, enantiomer 2: 34.28 min.

*3.5.10. (S)-4-tert-Butyl-3-((2S,3S)-2,3-diphenylpent-4-enoyl)-oxazolidin-2-one, (+)-****6j****.* General procedure B performed on a 0.12 mmol scale. The crude product (90:10 *syn*/*anti* as determined

by $^1$H NMR analysis) was purified by column chromatography (50% diethyl ether in hexanes) to afford *amide* (+)-**6j** (39 mg, 79%) as a white solid. $R_f$ 0.52 (50% diethyl ether in hexanes); mp 176–178 °C; $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.22–7.19 (m, 2H, Ar*H*), 7.11–7.02 (m, 8H, Ar*H*), 6.19 (ddd, 1H, *J*=17.4, 9.7, 7.7 Hz, $CH_2$=C*H*), 5.71 (d, 1H, *J*=11.4 Hz, C(O)C*H*), 5.32 (d, 1H, *J*=17.2 Hz, CH=C*H*$^{trans}$H$^{cis}$), 5.16 (d, 1H, *J*=10.3 Hz, CH=CH$^{trans}$*H*$^{cis}$), 4.36 (dd, 1H, *J*=7.6, 1.3 Hz, $CH_2$=CHC*H*), 4.22–4.19 (m, 2H, O$CH_2$), 4.02 (dd, 1H, *J*=9.2, 7.6 Hz, NC*H*), 0.98 (s, 9H, *t-Bu*); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 173.0, 154.5, 140.5, 139.8, 136.4, 129.4, 128.5, 128.2, 128.1, 127.1, 126.3, 116.0, 64.9, 61.9, 53.9, 52.4, 35.8, 25.9; $\nu_{max}$ (film)/cm$^{-1}$ 2961, 1759, 1703, 1370, 1212, 1184, 1106; $[\alpha]_D^{25}$ +13.5 (*c* 0.1, $CHCl_3$); HRMS ($ES^+$) mass calcd for $C_{24}H_{27}NO_3$ [$(M+NH_4)^+$]: 395.2329; found: 395.2324.

*3.5.11. (S)-4-(tert-butyl)-3-((R)-2-((S)-1-phenylallyl)octanoyl)-oxazolidin-2-one, (+)-**6k**.* General procedure B performed on a 0.13 mmol scale. The crude product (91:9 *syn*/*anti* as determined by $^1$H NMR analysis) was purified by column chromatography (20% diethyl ether in hexanes) to afford *amide* (+)-**6k** (39 mg, 79%) as a colourless oil. $R_f$ 0.69 (50% diethyl ether in hexanes); $^1$H NMR (400 MHz, chloroform-$d_1$) $\delta$ 7.33–7.26 (m, 4H, Ph*H*), 7.23–7.20 (m, 1H, Ph*H*), 6.16 (ddd, 1H, *J*=17.1, 9.9, 7.3 Hz, $CH_2$=C*H*), 5.15 (dd, 1H, *J*=16.4, 0.9 Hz, CH=C*H*$^{trans}$H$^{cis}$), 5.00 (dd, 1H, *J*=10.2, 1.5 Hz, CH=CH$^{trans}$*H*$^{cis}$), 4.50 (td, 1H, *J*=10.6, 7.1 Hz, C(O)C*H*), 4.44 (dd, 1H, *J*=7.5, 0.9 Hz, NC*H*), 4.30 (dd, 1H, *J*=9.2, 0.9 Hz, OCH*H*′), 4.17 (dd, 1H, *J*=9.1, 7.6 Hz, OC*H*H′), 3.53 (t, 1H, *J*=9.8 Hz, PhC*H*), 1.18–1.06 (m, 10H, $(CH_2)_5CH_3$), 0.95 (s, 9H, *t-Bu*), 0.80 (t, 3H, *J*=6.9 Hz, $(CH_2)_5CH_3$); $^{13}$C NMR (100 MHz, chloroform-$d_1$) $\delta$ 175.9, 154.9, 142.1, 139.9, 128.7, 128.0, 126.6, 116.0, 65.8, 65.3, 62.1, 54.4, 46.5, 35.9, 31.6, 29.1, 27.0, 25.9, 22.5, 15.2, 14.0; $\nu_{max}$ (film)/cm$^{-1}$ 2923, 1778, 1700, 1370, 1319, 1182, 1100; $[\alpha]_D^{25}$ +28.6 (*c* 1.0, $CHCl_3$); HRMS ($ES^+$) mass calcd for $C_{24}H_{35}NO_3$ [$(M+H)^+$]: 386.2685; found: 386.2687.

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## Supplementary data

Spectral data and compound characterization are available as Supplementary data free of charge via the Internet. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.05.045.

## References and notes

1. (a) *Modern Aldol Reactions*; Mahrwald, R., Ed.; Wiley-VCH: Weinheim, Germany, 2004; (b) Mukaiyama, T. *Org. React.* **1982**, *28*, 203; (c) Cowden, C. J.; Paterson, I. *Org. React.* **1997**, *51*, 1; (d) Kim, B. M.; Williams, S. F.; Masamune, S. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: London, 1991; (e) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1.
2. For reviews see: (a) Shibasaki, M. *Multimetallic Catalysis in Organic Synthesis*; Wiley-VCH: Weinhem, 2004; (b) Shibasaki, M.; Yoshikawa, N. *Chem. Rev.* **2002**, *102*, 2187; (c) Johnson, J. S.; Evans, D. A. *Acc. Chem. Res.* **2000**, *33*, 325; (d) For recent examples, please see Shibasaki, M.; Sasai, H.; Arai, T. *Angew. Chem., Int. Ed.* **1997**, *36*, 1236; (e) Trost, B. M.; Müller, C. *J. Am. Chem. Soc.* **2008**, *130*, 2438 and references therein; (f) Northrup, A. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 6798.
3. For examples of multi-catalytic systems, see: (a) Cernak, T. A.; Lambert, T. H. *J. Am. Chem. Soc.* **2009**, *131*, 3124; (b) Kelly, B. D.; Allen, J. M.; Tundel, R. E.; Lambert, T. H. *Org. Lett.* **2009**, *11*, 1381; (c) Evans, P. A.; Cui, J.; Gharpure, S. J.; Hinkle, R. J. *J. Am. Chem. Soc.* **2003**, *125*, 11456.
4. (a) Suzuki, T.; Tokunaga, M.; Wakatsuki, Y. *Org. Lett.* **2001**, *3*, 735; (b) Ackermann, L.; Kaspar, L. T. *J. Org. Chem.* **2007**, *72*, 6149; (c) Clay, J. M.; Vedejs, E. *J. Am. Chem. Soc.* **2005**, *127*, 5766; (d) Kabalka, G. W.; Shoup, T. M.; Goudgaon, N. M. *J. Org. Chem.* **1989**, *54*, 5930; (e) Chen, Y.; Ho, D. M.; Lee, C. *J. Am. Chem. Soc.* **2005**, *127*, 12184; (f) Marion, N.; Ramon, R.; Nolan, S. P. *J. Am. Chem. Soc.* **2009**, *131*, 448.
5. Witham, C. A.; Mauleon, P.; Shapiro, N. D.; Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 5838.
6. For examples, see: (a) Saito, N.; Katayama, T.; Sato, Y. *Org. Lett.* **2008**, *10*, 3829; (b) Gourdet, B.; Lam, H. W. *J. Am. Chem. Soc.* **2009**, *131*, 3802; (c) Das, J. P.; Chechlik, H.; Marek, I. *Nat. Chem.* **2009**, *1*, 128.
7. For a review of ynamide chemistry: Zificsak, C. A.; Mulder, J. A.; Hsung, R. P.; Rameshkumar, C.; Wei, L. L. *Tetrahedron* **2001**, *57*, 7575.
8. Yamamoto, H.; Futatsugi, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 1924.
9. Sun, J.; Kozmin, S. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4991.
10. See Supplementary data for details.
11. (a) Evans, D. A.; Tedrow, J. S.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2002**, *124*, 392; (b) Evans, D. A.; Downey, C. W.; Shaw, J. T.; Tredow, J. S. *Org. Lett.* **2002**, *4*, 1127; (c) Saito, S.; Kobayashi, S. *J. Am. Chem. Soc.* **2006**, *128*, 8704.
12. (a) Ficini, J.; Lumbroso-Bader, N.; Pouliquen, J. *Tetrahedron Lett.* **1968**, *39*, 4139; (b) Ficini, J.; Barbara, C. *Tetrahedron Lett.* **1966**, *52*, 6425; (c) Martin Castro, A. M. *Chem. Rev.* **2004**, *104*, 2939.
13. Mulder, J. A.; Hsung, R. P.; Frederick, M. O.; Tracey, M. R.; Zificsak, C. A. *Org. Lett.* **2002**, *4*, 1383.
14. As the metal triflate catalyst controls the release of TfOH (see Experimental for details) it is possible that the reaction is catalyzed solely by the Brønsted acid. However, the use of solely catalytic amounts of TfOH only provides the rearranged product in <10% yield (cf. 88% with the catalytic metal triflate).
15. For recent examples of catalytic [3,3]-Claisen-type rearrangements, see: (a) Nelson, S. G.; Wang, K. *J. Am. Chem. Soc.* **2006**, *128*, 4232; (b) Bourgeois, D.; Craig, D.; King, N. P.; Mountford, D. M. *Angew. Chem., Int. Ed.* **2004**, *44*, 618; (c) Akiyama, K.; Mikami, K. *Tetrahedron Lett.* **2004**, *45*, 7217; (d) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978; (e) Nelson, S. G.; Bungard, C. J.; Wang, K. *J. Am. Chem. Soc.* **2003**, *125*, 13000; (f) Hiersemann, M.; Abraham, L. *Eur. J. Org. Chem.* **2002**, 1461; (g) Uyeda, C.; Jacobsen, E. *J. Am. Chem. Soc.* **2008**, *130*, 9228; (h) Linton, E. C.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 16162; (i) Yoon, T. P.; Dong, V. M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **1999**, *121*, 9726.
16. Frederick, M. O.; Mulder, J. A.; Tracey, M. R.; Hsung, R. P.; Huang, J.; Kurtz, K. C. M.; Shen, L.; Douglas, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 2368.