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Substrate scope and stereocontrol in the Rh(II)-catalysed oxyamination of allylic carbamates

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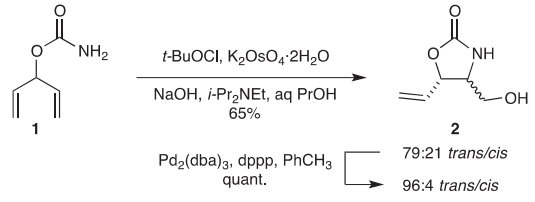
ABSTRACT

Application of a modified Du Bois protocol for rhodium-stabilised nitrenoid generation to a variety of allylic carbamates results in 4-acetoxymethyl-1,3-oxazolidin-2-one derivatives with moderate to high levels of stereocontrol.

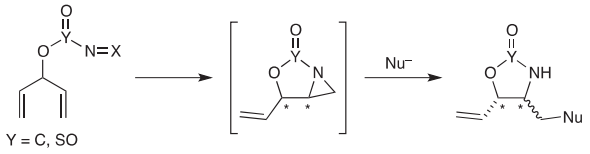
1. Introduction

Exploratory work concerning the stereoselective synthesis of biologically active aminopolyols led us to evaluate tethered aminohydroxylation (TA)[1] and related processes from dienyl carbamates and sulfamates. Thus, with 1,2-dienyl (allenyl) substrates, iminocyclopropane adducts were obtained from sulfamates[2] and bicyclic methylene aziridines from carbamates.[3] In a second line of investigation, the novel 1,4-dienyl carbamate **1** (Scheme 1),[4] prepared from divinyl carbinol using the standard procedure,[5] was subjected to the published TA conditions to give oxazolidinone **2** (79:21 *trans*/*cis* ratio) in 65% unoptimised yield.[6] The *dr* was raised to 96:4 by Pd(0)-mediated equilibration[7] and pure *trans*-**2** was obtained by recrystallisation from ethyl acetate. This versatile intermediate was then applied in an approach to the glycosidase inhibitor nagstatin[6] and a concise synthesis of (±)-safingol.[4]

With the intention of developing alternatives to the published route to (*R*,*R*)- and (*S*,*S*)-**2** from serine enantiomers,[8] and considering that an asymmetric TA variant was not available, we considered a related intramolecular aziridination/ring-opening process (Scheme 2). This was expected to offer opportunities for controlling the absolute stereochemistry and, in broader applications, would provide an overall *anti*-1,2-aminohydroxylation of the alkene in contrast to the *syn*-stereospecific TA. Intramolecular aziridination by thermal or photochemical loss of nitrogen from azidoformates[9] was discounted on the basis of limited prospects for achieving asymmetric variants. This left a choice between sulfamates[10] and carbamates[11] as aziridination precursors, from which nitrenoid reactive intermediates may be generated by oxidation, usually with



Scheme 1.



Scheme 2.

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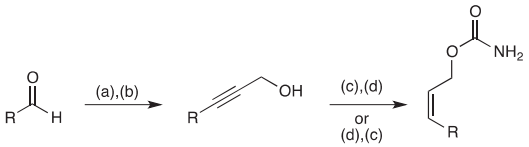
an iodine(III) reagent, and complexation, for example, with a rhodium(II) or copper(I) catalyst.[12] Finally, because allylic sulfamates are relatively unstable, we focused on carbamate substrates (Y=C in Scheme 2).

Application of Du Bois' original conditions for CH-insertion reactions[13] [PhI(OAc)$_2$, Rh$_2$(OAc)$_4$ or Rh$_2$(TPA)$_4$, MgO, CH$_2$Cl$_2$, 40 °C] to alkene aziridination delivers either intact aziridines, or products of ring-opening by acetate liberated from the I(III) oxidant.[11,14] The balance seems to be a fine one with glycal- and indole-derived aziridines opening readily (S_N1-like), with carbocyclic alkene-derived aziridines requiring higher temperatures. The aziridine is retained in oxazolidinone-fused products when prepared by Lebel's *N*-sulfonyloxycarbamate modification that requires no external oxidant,[15] and in oxazinanone-fused products generated from homoallylic carbamates using PhIO as the oxidant.[11f] The recently-reported Fe(II)-mediated transformation of allylic *N*-acyloxycarbamates into 4-(acyloxyalkyl)oxazolidinones may also yield intact aziridines when the reaction is performed at 0 °C;[16] this reaction shows promising enantioselectivity in selected cases but is not stereospecific.

In light of this extensive background, it was surprising that a systematic study of Du Bois-type aziridination, coupled with ring-opening in situ by acetate present in the reaction mixture, had not been reported and, to the best of our knowledge, this is still the case. Given the potential application of this method in the synthesis of aminoalcohols we set out to establish whether the reaction is stereospecific or usefully stereoselective, and whether the application of known chiral Rh(II) catalysts would provide acceptable enantiomeric enrichment. The results of this study are presented herein.

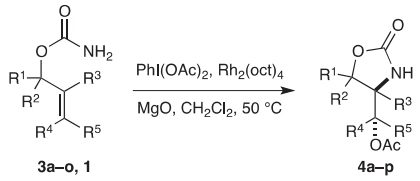
2. Results and discussion

As mentioned, prior to this study, the precedent for acetoxyamination via an allylic carbamate was confined to the reactions of electron-rich glycal or indole substrates in which the acetolysis follows a stepwise elimination/addition pathway. Thus, we selected a range of simple alkenyl substrates that would reveal the inherent diastereoselectivity and regioselectivity of the process. Precursor alcohols were either commercially available or, in the case of (*Z*)-1,2-disubstituted(alkenyl) alcohols, prepared by standard literature procedures. For example, Lindlar catalysed partial hydrogenation of propargyl alcohols, obtained via a Corey–Fuchs sequence from the appropriate aldehydes,[17] gave the corresponding alkenols (Scheme 3). In our hands the hydrogenations were not reliably stereoselective and *Z*/*E* mixtures were obtained in most cases. For the purposes of this investigation the levels of enrichment in the *Z*-isomer were deemed sufficient.



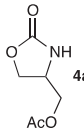
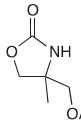
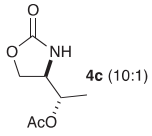
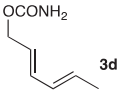
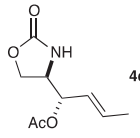
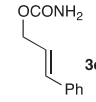
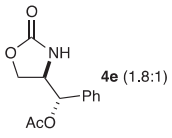
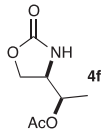
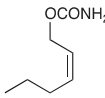
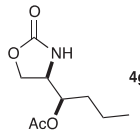
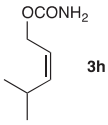
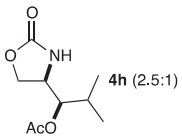
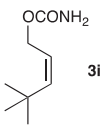
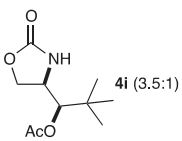
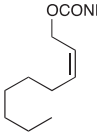
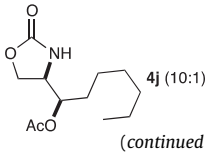
Scheme 3. Reagents and conditions: (a) CBr$_4$, PPh$_3$, CH$_2$Cl$_2$, 0 °C; (b) BuLi, THF, −78 °C then (HCHO)$_n$, THF, −78 °C to rt; (c) Cl$_3$CCONCO, CH$_2$Cl$_2$, 0 °C then K$_2$CO$_3$, aq MeOH; (d) H$_2$, Lindlar's catalyst, quinoline, MeOH.

With these substrates (**3a**–**o**, **1**), a slight modification to the original Du Bois conditions—increasing the temperature to 50 °C and using the more organic soluble Rh$_2$(oct)$_4$ in place of Rh$_2$(OAc)$_4$—resulted in all cases in the formation of 4-(acetoxymethyl)oxazolidinones **4a**–**p** (Scheme 4 and Table 1). Apart from oxazolidinone **4a**[18] (entry 1), all products are novel compounds and



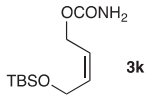
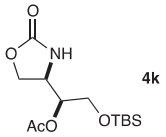
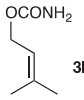
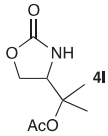
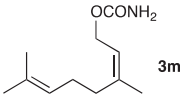
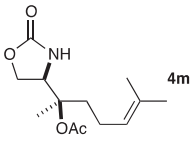
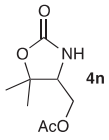
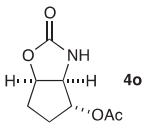
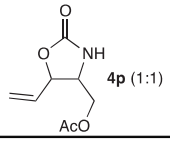
Scheme 4.

Table 1
Oxyamination outcomes according to Scheme 4

Entry	Carbamate (*dr*)[a]	Major product (*dr*)[a]	Yield %
1	 **3a**	 **4a**	75
2	 **3b**	 **4b**	62
3	 **3c** (16:1)	 **4c** (10:1)	64
4	 **3d**	 **4d**	61
5	 **3e**	 **4e** (1.8:1)	48
6	 **3f** (5:1)	 **4f** (3:1)	46
7	 **3g**	 **4g**	60
8	 **3h** (3:1)	 **4h** (2.5:1)	46
9	 **3i** (5:1)	 **4i** (3.5:1)	53
10	 **3j**	 **4j** (10:1)	75

(*continued on next page*)

Table 1 (*continued*)

Entry	Carbamate (*dr*)[a]	Major product (*dr*)[a]	Yield %
11	 **3k**	 **4k**	69
12	 **3l**	 **4l**	64
13	 **3m**	 **4m**	56
14	 **3n**	 **4n**	60
15	 **3o**	 **4o**	50
16	 **1**	 **4p** (1:1)	46

[a] Diastereomeric ratios refer to major : minor as judged by comparisons of integral values in the ^{1}H NMR spectra; only the major isomers are depicted and where a *dr* is not given, essentially a single diastereomer was observed. For **4a**–**p**, the quoted *dr* in each case refers to that present in the crude product mixture.

the relative stereochemistry was confirmed in selected cases, see below.

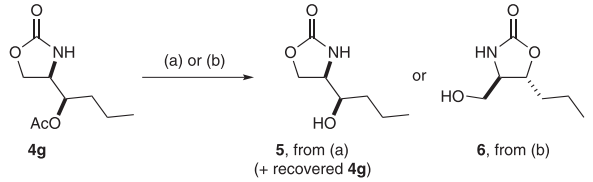
From the table, several key points emerge:

(a) Oxazolidinones **4a**–**p** are formed with excellent conversion, and the yields are comparable to those reported for indole and glycal substrates.

(b) Acetolysis of the intermediate aziridines is completely regioselective, proceeding via cleavage of the *exo*-C–N bond to form oxazolidinones (cf. Scheme 2) rather than via *endo*-C–N cleavage and oxazinanone formation. This is the normal ring-opening mode for carbamate-derived bicyclic aziridines, expected on the basis of effective delocalisation of the C–N bonding electrons into the roughly parallel C=O π-system as the addition progresses.

(c) The reactions retain most but by no means all of the stereochemical integrity (*E*/*Z*) of the precursors. For example, the reaction of the sorbyl substrate **3d** proceeds with a high degree of stereospecificity, but the *E*-crotyl substrate **3c** suffers an erosion in *dr* during the aziridination and acetolysis from 16:1 to 10:1. The situation is more pronounced in the cinnamyl example **3e** where an erosion of the *dr* may more easily arise from an S_N1-like acetolysis. In the *Z*-1,2-disubstituted cases, the unbranched alkyl substrates **3g**, **3j**, and **3k** gave products essentially as single diastereoisomers; the methyl (**3f**) and the branched alkyl substrates **3h** and **3i** proceeded with a small erosion in *dr*.

(d) The stereospecificity arises formally by concerted aziridination, and S_N2-like acetolysis of the *exo*-C–N bond. This was supported initially by comparison of the reactions of *E*-**3c** and *Z*-**3f**, which provided opposite major:minor diastereomeric products **4c** and **4f**, respectively. Confirmation of the stereochemistry of **4g** was obtained by effecting partial hydrolysis of the acetate with aq NaOH in THF to give alcohol **5** (Scheme 5) with the NMR data matching those published.[1e] The reaction had to be quenched prior to completion in order to limit competing acyl transfer; with aq LiOH and a longer reaction time, complete conversion to regioisomer **6**[19] resulted.



Scheme 5. Reagents and conditions: (a) NaOH, aq THF, 4 h; (b) LiOH, aq THF, 23 h.

(e) Further substitution at the alkene terminus (substrates **3l** and **3m**) or at the carbamate α-position (**3n**) is well-tolerated, with the reaction of neryl carbamate **3m** affording essentially a single diastereoisomer. It was disappointing that the reaction of our original pentadienyl carbamate (**1**, entry 16) showed no apparent facial bias during the aziridination, leading to a 1:1 mixture of *cis*- and *trans*-oxazolidinones **4p**.

(f) The results from substrates **3d** and **3o** are noteworthy because the yields reported for the analogous TA reactions are 41% for **3d**[1a] and for **3o** the reaction failed completely.[1b]

We briefly explored the possibility of effecting the reaction in the presence of added nucleophiles that may out-compete acetate for aziridine ring-opening. The addition of 1.0 mol equivalent of methanol in the reaction of prenyl carbamate (**3l**) had little effect, the obtained oxazolidinone consisting entirely of the acetoxymethyl derivative **4l**; using a five-fold excess of methanol returned a roughly 1:1 mixture of methoxy- (**7**, Fig. 1) and acetoxy- (**4l**) products. With the same substrate (**3l**), and 5.0 equiv of water, the reaction was largely suppressed and only a 20% conversion, to the acetoxy-product **4l**, resulted. The addition of 5.0 equiv of diethylamine or 5.0 equiv of sodium azide led to the complete recovery of starting material. However, results with substrates such as alcohol **8** bearing an internal nucleophile, specifically a 3-hydroxypropyl-substituent, led to bicyclic products of the form **9**; these will be reported separately.[20]

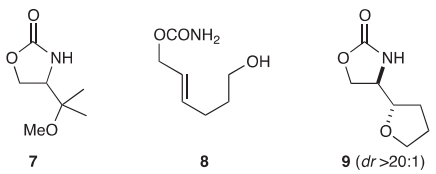


Fig. 1. Products arising from inter- (**7**) and intra-molecular (**9**, from substrate **8**) alkoxyamination.

3. Conclusion

An operationally simple and reliable procedure for the acetoxyamination of a broad range of allylic carbamates has been established. These reactions result in the formation of two contiguous stereocentres from readily available starting materials, and proceed with high diastereocontrol and complete regiocontrol. The opportunity to develop asymmetric variants of these procedures, using any of the increasing number of known chiral dirhodium catalysts,[21] enhances the value of this methodology and is an obvious objective for future work in this field.[22]

4. Experimental section

4.1. General aspects

Commercially available reagents were dried and purified before use where appropriate using standard procedures. 'Petrol' refers to the fraction of petroleum ether boiling in the range 30–40 °C; ether refers to diethyl ether; methanol and dichloromethane were dried by passing through activated alumina under argon. All other solvents and reagents were used as supplied without prior purification. Reactions were routinely carried out in oven-dried glassware under an argon atmosphere. Diastereomeric ratios (*dr*) were calculated from the integration of ^{1}H NMR resonances. Thin layer chromatography was performed using Merck aluminium-backed 0.2 mm Kieselgel 60 F_{254} pre-coated plates. Plates were visualised by the quenching of ultraviolet fluorescence (λ_{max} 254 nm) then stained and heated with either anisaldehyde or potassium permanganate. Retention factors (R_f) are reported with the solvent system used in parentheses. Flash column chromatography was performed on Merck 60 silica with a particle size of 40–63 μm; the solvent system is given in parentheses. Melting points were determined using a Griffin heated metal block apparatus and are uncorrected. Infrared spectra were recorded as thin films on NaCl disks using a Perkin–Elmer Paragon 1000 FT-IR spectrophotometer or a Bruker Tensor 27 FT-IR. Absorption maxima (ν_{max}) are given in wavenumbers (cm^{-1}) and are classified as strong (s), medium (m), weak (w) and broad (br). Proton (^{1}H) NMR spectra were recorded on the following spectrometers: Bruker AVC-500 (500 MHz); Bruker DQX-400 or DPX-400 (400 MHz); Bruker DPX-200 (200 MHz). Assignments were made on the basis of chemical shift and coupling constants using COSY and NOE experiments where appropriate. Abbreviations used in the description of multiplicities are singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), sextet (sext), multiplet (m), apparent (app) and broad (br). Coupling constants (*J*) are quoted to the nearest 0.1 Hz. Carbon-13 (^{13}C) NMR spectra were recorded on the following spectrometers: Bruker AVC-500 (125 MHz); Bruker DQX-400 or DPX-400 (100 MHz). Assignments were made on the basis of DEPT, HMBC and HSQC experiments as appropriate. High resolution mass spectra (HRMS) were recorded using a Micromass GCT (CI), a Micromass AutoSpec-oaTOF (CI or EI), or a Micromass LCT (ESI). Mass to charge ratios (*m*/*z*) are reported in Daltons. Known carbamates **3a**–**e**, **3g**, **3l**, and **3m** were prepared by the standard procedure from the corresponding alcohol.[5]

4.2. General procedure for synthesis of oxyamination substrates

Trichloroacetyl isocyanate (1.0 mL, 8.46 mmol) was added dropwise to a stirred solution of the alcohol (7.05 mmol) in dry dichloromethane (15.0 mL) at 0 °C. After stirring for 1 h the mixture was concentrated in vacuo, dissolved in methanol (20 mL) and cooled to 0 °C. K_2CO_3 solution (aq, 2.0 M, 10 mL) was added, and the mixture was warmed to RT then stirred for 3 h. The methanol was evaporated and the remaining aqueous residue extracted with dichloromethane (3×20 mL). The combined organic extracts were concentrated in vacuo and purified by column chromatography (petrol/ethyl acetate, 4:1) to give the carbamates (**1**, **3a**–**o**). As an alternative work-up, the crude reaction mixture was loaded onto a pad of basic alumina and allowed to stand for 5 min before flushing through with ethyl acetate and concentrating in vacuo.

4.3. Penta-1,4-dien-3-yl carbamate (1)[6]

White solid (4.84 g, 86%). R_f 0.55 (ethyl acetate); mp 40–42 °C; ν_{max} (thin film)/cm^{-1} 3432s, 3274m, 3214m, 1688s, 1614s, 1410s, 1289w; δ_H (400 MHz, $CDCl_3$) 4.72 (2H, br s, NH_2), 5.22 (2H, d, *J* 10.4 Hz) and 5.30 (2H, d, *J* 17.2 Hz, 2× =CH_2), 5.57–5.60 (1H, m, OCH), 5.84 (2H, ddd, *J* 17.2, 10.4, 5.8 Hz, 2× C*H*=CH_2); δ_C (100 MHz, $CDCl_3$) 75.6 (CH), 117.2 (CH_2), 135.3 (CH), 156.3 (C); HRMS (CI$^+$) found 128.0713, $C_6H_{10}NO_2$ (MH$^+$) requires 128.0712.

4.4. (*Z*)-But-2-enyl carbamate (3f)

White solid (77 mg, 82%), a mixture of geometrical isomers (*Z*/*E*, 5:1). R_f 0.70 (ethyl acetate); mp 40–42 °C; ν_{max} (thin film)/cm^{-1} 3352br, 3030w, 2946w, 1714s, 1602m, 1394w, 1322s, 1057m, 785w; δ_H (400 MHz, $CDCl_3$) Data for the *Z*-isomer: 1.70 (3H, d, *J* 7.0 Hz, CH_3), 4.63 (2H, d, *J* 6.8 Hz, OCH_2), 4.80 (2H, br s, NH_2), 5.52–5.59 (1H, m, CH_2CH), 5.68–5.75 (1H, m, $CHCH_3$); δ_C (100 MHz, $CDCl_3$) 13.1 (CH_3), 60.7 (CH_2), 124.5 (CH), 129.5 (CH), 157.6 (C); HRMS (ESI$^+$) found 138.0535, $C_5H_9NNaO_2$ (MNa$^+$) requires 138.0525.

4.5. (*Z*)-4-Methylpent-2-enyl carbamate (3h)

White solid (from partial hydrogenation of the corresponding propargylic carbamate); a fraction of *dr*=20:1, obtained by chromatography on $AgNO_3$-impregnated silica, was used for characterisation. R_f 0.67 (ethyl acetate); mp 38–40 °C; ν_{max} (thin film)/cm^{-1} 3411br, 3026w, 2956m, 1683s, 1486m, 1121m, 801w, 725w; δ_H (500 MHz, $CDCl_3$) 0.96 (6H, d, *J* 6.6 Hz, 2× CH_3), 2.61–2.70 (1H, m, $CH(CH_3)_2$), 4.62 (2H, d, *J* 6.0 Hz, OCH_2), 4.73 (2H, br s, NH_2), 5.39–5.50 (2H, m, CH=CH); δ_C (125 MHz, $CDCl_3$) 23.0 (CH_3), 27.0 (CH), 61.1 (CH_2), 121.1 (CH), 142.6 (CH), 156.9 (C); HRMS (CI$^+$) found 143.0939, $C_7H_{13}NO_2$ (MH$^+$) requires 143.0946.

4.6. (*Z*)-4,4-Dimethylpent-2-enyl carbamate (3i)

Colourless oil (52 mg, 51%), a mixture of geometrical isomers (*Z*/*E*, 5:1). R_f 0.56 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3347br, 1716s, 1379w, 1324m, 1055m; δ_H (500 MHz, $CDCl_3$) 1.13 (9H, s, $C(CH_3)_3$), 4.60 (2H, br s, NH_2), 4.78 (2H, d, *J* 6.4 Hz, OCH_2), 5.31 (1H, dt, *J* 12.3, 6.4 Hz, CH_2CH), 5.53 (1H, d, *J* 12.3 Hz, $CHC(CH_3)_3$); δ_C (125 MHz, $CDCl_3$) 30.8 (CH_3), 33.6 (C), 61.8 (CH_2), 122.3 (CH), 143.9 (CH), 156.6 (C); HRMS (ESI$^+$) found 180.0992, $C_8H_{15}NNaO_2$ (MNa$^+$) requires 180.0995.

4.7. (*Z*)-Non-2-enyl carbamate (3j)

Colourless oil (1.19 g, 91%). R_f 0.66 (ethyl acetate); ν_{max} (thin film)/ cm^{-1} 3350br, 2928s, 2856w, 1713s, 1601w, 1458w, 1387m, 1328m, 1053m, 784w; δ_H (400 MHz, $CDCl_3$) 0.87 (3H, t, *J* 6.4 Hz, CH_3), 1.21–1.37 (8H, m, $C_4H_8CH_3$), 2.08 (2H, app q, *J* 7.0 Hz, =$CHCH_2$), 4.60 (2H, d, *J* 6.8 Hz, OCH_2), 4.99 (2H, br s, NH_2), 5.47–5.55 (1H, m, OCH_2CH=), 5.58–5.66 (1H, m, =$CHCH_2$); δ_C (100 MHz, $CDCl_3$); 14.0 (CH_3), 22.6 (CH_2), 27.5 (CH_2), 28.8 (CH_2), 29.4 (CH_2), 31.6 (CH_2), 61.0 (CH_2), 123.5 (CH), 135.3 (CH), 157.2 (C); HRMS (ESI$^+$) found 208.1309, $C_{10}H_{19}NNaO_2$ (MNa$^+$) requires 208.1308.

4.8. (*Z*)-4-(*tert*-Butyldimethylsilyloxy)but-2-enyl carbamate (3k)

Pale yellow oil (606 mg, 52%); ν_{max} (thin film)/cm^{-1} 3355br, 2930m, 2850w, 1717s, 1603w, 1390m, 1319m, 1256w, 1065s, 838m, 778w; δ_H (400 MHz, $CDCl_3$) 0.08 (6H, s, $Si(CH_3)_2$), 0.90 (9H, s, $C(CH_3)_3$), 4.64 (2H, d, *J* 5.8 Hz) and 4.74 (2H, d, *J* 6.6 Hz, 2× OCH_2), 4.74 (2H, br s, NH_2), 5.53–5.62 (1H, m) and 5.70–5.77 (1H, m, CH=CH); δ_C (100 MHz, $CDCl_3$) −5.2 (CH_3), 18.3 (C), 25.9 (CH_3), 59.5 (CH_2), 61.0 (CH_2), 124.3 (CH), 133.3 (CH), 156.6 (C); HRMS (ESI$^+$) found 268.1339, $C_{11}H_{23}NNaO_3Si$ (MNa^+) requires 268.1339.

4.9. 2-Methylbut-3-en-2-yl carbamate (3n)

White solid (302 mg, 83%). R_f 0.62 (ethyl acetate); mp 56–58 °C; ν_{max} (KBr)/cm^{-1} 3458m, 2360w, 1686s, 1603w, 1379m, 1133m, 1036w; δ_H (400 MHz, $CDCl_3$) 1.53 (6H, s, 2× CH_3), 4.59 (2H, br s, NH_2), 5.08 (1H, dd, *J* 10.9, 0.7 Hz) and 5.17 (1H, dd, *J* 17.5, 0.7 Hz, =CH_2), 6.12 (1H, dd, *J* 17.5, 10.9 Hz, CH=); δ_C (100 MHz, $CDCl_3$) 26.7 (CH_3), 80.1 (C), 112.4 (CH_2), 142.9 (CH), 155.9 (C); HRMS (ESI$^+$) found 152.0681, $C_6H_{11}NNaO_2$ (MNa^+) requires 152.0682.

4.10. General procedure for intramolecular oxyamination

A solution of the *O*-allyl carbamate (**1**, **3a**–**o**; 0.50 mmol) in dichloromethane (3.0 mL) was placed in a sealable pressure vessel and the headspace was purged with argon. MgO (56.0 mg, 1.66 mmol), diacetoxyiodobenzene (280 mg, 0.84 mmol), and rhodium(II) octanoate dimer (19.5 mg, 0.025 mmol) were added sequentially under a flow of argon. The reaction mixture was stirred vigorously at 50 °C for 18 h. The solution was cooled, the solvent was removed in vacuo, and the resulting solid residue was purified by column chromatography through a short plug of silica (petrol→petrol/ethyl acetate, 3:1→petrol/ethyl acetate, 1:1) giving oxazolidinones **4a**–**p**.

4.11. (2-Oxooxazolidin-4-yl)methyl acetate (4a)[18]

Colourless oil (59 mg, 75%) from carbamate **3a**. R_f 0.13 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3301br, 1740s, 1413w, 1235m, 1045m, 936w, 770w; δ_H (400 MHz, $CDCl_3$) 2.10 (CH_3), 4.03–4.20 (4H, m, O*CH*$_2$*CHCH*H′) 4.50 (1H, app t, *J* 8.5 Hz, OCH_2CHCH*H*′), 6.55 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$); 20.6 (CH_3), 51.1 (CH), 64.9 (CH_2), 66.9 (CH_2), 159.8 (C), 170.8 (C) [lit.[18] 20.7, 51.1, 64.9, 66.9, 159.8, 170.8].

4.12. (4-Methyl-2-oxooxazolidin-4-yl)methyl acetate (4b)

Colourless oil (27 mg, 62%) from carbamate **3b**. R_f 0.28 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3288br, 1743s, 1381w, 1237m, 1046m; δ_H (400 MHz, $CDCl_3$) 1.39 (3H, s, CCH_3), 2.12 (3H, s, $COCH_3$), 3.98 (1H, d, *J* 11.5 Hz, *CH*H′OAc), 4.07 (1H, d, *J* 8.8 Hz, OC*H*H′), 4.13 (1H, d, *J* 11.5 Hz, CH*H*′OAc), 4.29 (1H, d, *J* 8.8 Hz, OCH*H*′), 6.04 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 20.7 (CH_3), 23.0 (CH_3), 57.1 (C), 68.1 (CH_2), 73.0 (CH_2), 158.8 (C), 170.7 (C); HRMS (ESI$^+$) found 196.0573, $C_7H_{11}NNaO_4$ (MNa^+) requires 196.0580.

4.13. (*S**)-1-[(*R**)-2-Oxooxazolidin-4-yl]ethyl acetate (4c)

Pale yellow viscous oil (66 mg, 64%) from carbamate **3c**, with the same *dr* (10:1) as the crude product. R_f 0.22 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3288br, 1741s, 1413w, 1376w, 1239s, 1069m, 929w, 769w; δ_H (400 MHz, $CDCl_3$) 1.25 (3H, d, *J* 6.5 Hz, $CHCH_3$), 2.08 (3H, s, $COCH_3$), 3.94–3.99 (1H, m, NCH), 4.26 (1H, dd, *J* 8.9, 5.0 Hz) and 4.47 (1H, app t, *J* 8.9 Hz, OCH_2), 4.95–5.02 (1H, m, *CH*CH_3), 6.58 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 15.1 (CH_3), 21.0 (CH_3), 55.5 (CH), 66.2 (CH_2) 70.4 (CH), 160.0 (C), 170.4 (C); HRMS (ESI$^+$) found 196.0579, $C_7H_{11}NNaO_4$ (MNa^+) requires 196.0580.

4.14. (*S**,*E*)-1-[(*R**)-2-Oxooxazolidin-4-yl]but-2-enyl acetate (4d)

Colourless oil (61 mg, 61%) from carbamate **3d**. R_f 0.40 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3290br, 2920w, 1746s, 1409w, 1374m, 1232s, 1026m, 969w, 768w; δ_H (400 MHz, $CDCl_3$) 1.74 (3H, d, *J* 6.6 Hz, CH_3), 2.08 (3H, s, $COCH_3$), 4.00 (1H, app dt, *J* 8.9, 4.9 Hz, *CH*NH), 4.22 (1H, ddd, *J* 8.9, 4.9, 1.2 Hz) and 4.42 (1H, app td, *J* 8.9, 1.2 Hz, OCH_2), 5.20–5.25 (1H, m, *CH*OAc), 5.33–5.41 (1H, m, CHC*H*=), 5.85–5.94 (1H, m, *CH*CH_3), 6.05–6.20 (1H, m, NH); δ_C (100 MHz, $CDCl_3$) 18.0 (CH_3), 21.0 (CH_3), 54.6 (CH), 66.1 (CH_2), 74.7 (CH), 123.5 (CH), 133.9 (CH), 159.6 (C), 170.0 (C); HRMS (ESI$^+$) found 222.0738, $C_9H_{13}NNaO_4$ (MNa^+) requires 222.0737.

4.15. (*S**)- and (*R**)-[(*R**)-2-Oxooxazolidin-4-yl](phenyl) methyl acetate (4e)

Colourless viscous oil (57 mg, 48%) from carbamate **3e**, a mixture of diastereoisomers (A:B=63:37). R_f 0.31 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3285br, 1754s, 1408w, 1374w, 1231m, 1037m, 922w, 703w; δ_H (400 MHz, $CDCl_3$) 2.13 (3H, s, $COCH_3$, B), 2.15 (3H, s, $COCH_3$, A) 4.06–4.10 (1H, m, NCH, B), 4.17–4.40 (5H, m, OCH_2, A & B, NCH, A), 5.68 (1H, d *J* 7.5 Hz, *CH*Ph, B), 5.82 (1H, d, *J* 5.7 Hz, *CH*Ph, A), 5.83 (1H, br s, NH, A), 6.67 (1H, br s, NH, B), 7.31–7.42 (10H, m, Ph, A & B); δ_C (100 MHz, $CDCl_3$) 21.0 (CH_3, B), 21.0 (CH_3, A), 56.0 (CH, A), 56.2 (CH, B), 66.2 (CH_2, B), 66.3 (CH_2, A), 75.2 (CH, A), 77.1 (CH, B), 126.6 (CH, A), 127.1 (CH, B), 129.0 (two peaks), 129.1 and 129.2 (CH), 135.4 (C, A), 135.5 (C, B), 159.2 (C, A), 159.6 (C, B), 169.9 (C, A), 170.0 (C, B); HRMS (ESI$^+$) found 258.0740, $C_{12}H_{13}NNaO_4$ (MNa^+) requires 258.0737.

4.16. (*R**)-1-[(*R**)-2-Oxooxazolidin-4-yl]ethyl acetate (4f)

Pale yellow viscous oil (11 mg, 46%) from carbamate **3f**, with *dr*=3:1 in the crude product. R_f 0.22 (ethyl acetate); δ_H (400 MHz, $CDCl_3$) 1.24 (3H, d, *J* 6.3 Hz, CH_3), 2.10 (3H, s, $COCH_3$), 3.90–3.95 (1H, m, NCH), 4.17 (1H, dd, *J* 9.0, 5.2 Hz) and 4.48 (1H, app t, *J* 9.0 Hz, OCH_2), 4.86–4.92 (1H, m, *CH*CH_3), 5.77 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 15.6 (CH_3), 20.8 (CH_3), 55.7 (CH), 66.5 (CH_2), 71.1 (CH), 160.0 (C), 170.4 (C); HRMS (ESI$^+$) found 196.0579, $C_7H_{11}NNaO_4$ (MNa^+) requires 196.0580.

4.17. (*R**)-1-[(*R**)-2-Oxooxazolidin-4-yl]butyl acetate (4g)

Colourless oil (120 mg, 60%) from carbamate **3g**. R_f 0.42 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3279br, 2962m, 1743s, 1413w, 1375w, 1234s, 1028m, 919w, 732w; δ_H (400 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.3 Hz, CH_2CH_3), 1.23–1.60 (4H, m, C_2H_4), 2.10 (3H, s, $COCH_3$), 3.95 (1H, app dt, *J* 8.8, 5.2 Hz, *CH*NH), 4.14 (1H, dd, *J* 8.8, 5.2 Hz) and 4.43 (1H, app t, *J* 8.8 Hz, OCH_2), 4.92–4.96 (1H, m, *CH*OAc), 7.11 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 13.8 (CH_3), 18.4 (CH_2), 20.9 (CH_3), 32.4 (CH_2), 54.9 (CH), 66.8 (CH_2), 73.7 (CH), 160.3 (C), 170.9 (C); HRMS (ESI$^+$) found 224.0884, $C_9H_{15}NNaO_4$ (MNa^+) requires 224.0893.

4.18. (*R**)-2-Methyl-1-[(*R**)-2-oxooxazolidin-4-yl]propyl acetate (4h)

Colourless oil (21 mg, 46%) from carbamate **3h**, with *dr*=2.5:1 in the crude product from which a sample with *dr*>10:1 was obtained for characterisation. R_f 0.42 (ethyl acetate); ν_{max} (thin film)/ cm^{-1} 3274br, 1748s, 1374w, 1237s, 1026m, 768w; δ_H (500 MHz, $CDCl_3$) 0.93 (3H, d, *J* 6.6 Hz, CH_3), 0.97 (3H, d, *J* 6.8 Hz, CH_3), 1.82–1.89 (1H, m, *CH*$(CH_3)_2$), 2.15 (3H, s, $COCH_3$), 4.09–4.14 (2H, m, *CH*NH, OC*H*H′),

4.43–4.49 (1H, m, OCH*H*′), 4.76–4.79 (1H, m, C*H*OAc), 6.22 (1H, br s, NH); δ_C (125 MHz, $CDCl_3$) 17.9 (CH_3), 18.9 (CH_3) 20.7 (CH_3), 29.3 (CH), 53.1 (CH), 67.2 (CH_2), 78.0 (CH), 159.8 (C), 171.0 (C); HRMS (ESI^+) found 224.0894, $C_9H_{15}NNaO_4$ (MNa^+) requires 224.0893.

4.19. (*R**)-2,2-Dimethyl-1-[(*R**)-2-oxooxazolidin-4-yl]propyl acetate (4i)

Colourless oil (13 mg, 53%) from carbamate **3i**, with *dr*=3.5:1 in the crude product from which a sample with *dr*>10:1 was obtained for characterisation. R_f 0.44 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3282br, 2963m, 1761s, 1372w, 1236s, 1157w, 1051m, 913w, 809w; δ_H (500 MHz, $CDCl_3$) 0.96 (9H, s, $C(CH_3)_3$), 2.16 (3H, s, $COCH_3$), 4.12–4.19 (2H, m, C*H*NH, OC*H*H′), 4.48 (1H, app t, *J* 7.7 Hz, OCH*H*′), 4.75 (1H, d, *J* 3.6 Hz, C*H*OAc), 5.68 (1H, br s, NH); δ_C (125 MHz, $CDCl_3$) 20.7 (CH_3), 29.3 (CH_3), 34.1(C), 52.0 (CH), 68.8 (CH_2), 79.6 (CH), 159.5 (C), 170.8 (C); HRMS (ESI^+) found 238.1051, $C_{10}H_{17}NNaO_4$ (MNa^+) requires 238.1050.

4.20. (*R**)-1-[(*R**)-2-Oxooxazolidin-4-yl]heptyl acetate (4j)

Colourless oil (91 mg, 75%) from carbamate **3j**, with *dr*=10:1 in the crude product from which a sample with *dr*=11:1 was obtained for characterisation. R_f 0.32 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3274br, 1758s, 1412w, 1375m, 1236s, 1035m, 934w, 768w, 720w; δ_H (400 MHz, $CDCl_3$) 0.82–0.90 (3H, m, CH_3), 1.19–1.35 (8H, m, $C_4H_8CH_3$), 1.42–1.60 (2H, m, $CH_2C_5H_{11}$), 2.11 (3H, s, $COCH_3$), 3.92–4.00 (1H, m, NCH), 4.13 (1H, dd, *J* 8.8, 5.0 Hz) and 4.43 (1H, app t, *J* 8.8 Hz, OCH_2), 4.93 (1H, td, *J* 9.3, 1.2 Hz, C*H*OAc), 7.01 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 14.0 (CH_3), 20.9 (CH_3), 22.5 (CH_2), 25.0 (CH_2), 29.0 (CH_2), 30.3 (CH_2), 31.6 (CH_2), 54.9 (CH), 66.8 (CH_2), 74.0 (CH), 160.2 (C), 170.9 (C); HRMS (ESI^+) found 266.1352, $C_{12}H_{21}NNaO_4$ (MNa^+) requires 266.1363.

4.21. (*S**)-2-(*tert*-Butyldimethylsilyloxy)-1-[(*R**)-2-oxooxazolidin-4-yl]ethyl acetate (4k)

Pale yellow oil (104 mg, 69%) from carbamate **3k**. R_f 0.59 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3289br, 2930m, 1751s, 1472w, 1232s, 1114m, 838m, 779w; δ_H (500 MHz, $CDCl_3$) 0.08 (3H, s) and 0.08 (3H, s, $Si(CH_3)_2$), 0.90 (9H, s, $C(CH_3)_3$), 2.13 (3H, s, $COCH_3$), 3.74 (1H, dd, *J* 11.3, 5.0 Hz) and 3.82 (1H, dd, *J* 11.3, 3.6 Hz, CH_2OSi), 4.15–4.20 (1H, m, C*H*NH), 4.20–4.25 (1H, m) and 4.49 (1H, app t, *J* 8.7 Hz, OCH_2), 4.82–4.86 (1H, m, C*H*OAc), 5.78 (1H, br s, NH); δ_C (125 MHz, $CDCl_3$) −5.6 (CH_3), −5.4 (CH_3), 18.2 (C), 20.9 (CH_3), 25.8 (CH_3), 53.6 (CH), 62.7 (CH_2), 67.1 (CH_2), 73.6 (CH), 159.3 (C), 171.4 (C); HRMS (ESI^+) found 326.1393, $C_{13}H_{25}NNaO_5Si$ (MNa^+) requires 326.1394.

4.22. 2-(2-Oxooxazolidin-4-yl)propan-2-yl acetate (4l)

White solid (60 mg, 64%) from carbamate **3l**. R_f 0.12 (petrol/ethyl acetate, 2:1); mp 64–66 °C; ν_{max} (thin film)/cm^{-1} 3280br, 1737s, 1371m, 1245s, 1149m, 1022w, 994w, 770w, 721w; δ_H (400 MHz, $CDCl_3$) 1.46 and 1.48 (2×3H, s, 2× CH_3), 2.01 (3H, s, $COCH_3$), 4.05 (1H, dd, *J* 9.3, 4.9 Hz, C*H*NH), 4.26 (1H, dd, *J* 9.3, 4.9 Hz) and 4.42 (1H, app t, *J* 9.3 Hz, OCH_2), 6.97 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 20.8 (CH_3), 21.2 (CH_3), 22.2 (CH_3), 59.6 (CH), 65.9 (CH_2), 81.8 (C), 160.2 (C), 170.2 (C); HRMS (ESI^+) found 210.0733, $C_8H_{13}NNaO_4$ (MNa^+) requires 210.0737.

4.23. (*R**)-6-Methyl-2-[(*R**)-2-oxooxazolidin-4-yl]hept-5-en-2-yl acetate (4m)

Colourless oil (72 mg, 56%) from carbamate **3m**. R_f 0.41 (ethyl acetate); ν_{max} (thin film)/ cm^{-1} 3264br, 1760s, 1371w, 1241s, 1178w, 1130w, 1021m, 943w, 769w; δ_H (400 MHz, $CDCl_3$) 1.43 (3H, s, CH_3), 1.58 (3H, s, CH_3), 1.66 (3H, s, CH_3), 1.81–1.85 and 1.93–2.01 (4H, m, C_2H_4), 2.03 (3H, s, $COCH_3$), 4.11–4.19 (1H, m, OC*H*H′), 4.35–4.42 (2H, m, OCH*H*′, NHC*H*), 5.04 (1H, t, *J* 6.9 Hz, =CH), 6.88 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 17.6 (CH_3), 18.4 (CH_3), 21.8 (CH_2), 22.1 (CH_3), 25.6 (CH_3), 34.2 (CH_2), 57.4 (CH), 65.7 (CH_2), 84.4 (CH), 122.9 (CH), 132.6 (C), 160.1 (C), 170.4 (C); HRMS (ESI^+) found 278.1359, $C_{13}H_{21}NNaO_4$ (MNa^+) requires 278.1363.

4.24. (5,5-Dimethyl-2-oxooxazolidin-4-yl)methyl acetate (4n)

Colourless oil (56 mg, 60%) from carbamate **3n**. R_f 0.42 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3300br, 2982w, 1745s, 1375w, 1230m, 1044w; δ_H (400 MHz, $CDCl_3$) 1.41 (3H, s, CH_3), 1.51 (3H, s, CH_3), 2.10 (3H, s, $COCH_3$), 3.71 (1H, dd, *J* 7.9, 4.5 Hz, C*H*NH), 4.04 (1H, dd, *J* 11.3, 7.9 Hz) and 4.23 (1H, dd, *J* 11.3, 4.5 Hz, CH_2OAc), 6.29 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 20.7 (CH_3), 21.7 (CH_3), 28.0 (CH_3), 59.7 (CH), 63.3 (CH_2), 82.1 (C), 158.3 (C), 170.5 (C); HRMS (ESI^+) found 210.0728, $C_8H_{13}NNaO_4$ (MNa^+) requires 210.0737.

4.25. (3a*S**,4*R**,6a*R**)-2-Oxo-hexahydro-2*H*-cyclopenta[*d*]oxazol-4-yl acetate (4o)

Colourless oil (29 mg, 50%) from carbamate **3o**. R_f 0.41 (ethyl acetate); ν_{max} (thin film)/cm^{-1} 3300br, 1747s, 1375w, 1241m, 1169w, 1024m, 936w, 768w; δ_H (500 MHz, $CDCl_3$) 1.88–1.94 (1H, m, CH_2CHH'), 2.06 (3H, s, $COCH_3$), 2.06–2.13 (3H, m, CH_2CHH'), 4.04 (1H, app d, *J* 7.3 Hz, C*H*NH), 4.91 (1H, br s, CHOCO·N), 5.13 (1H, app dd, *J* 7.3, 5.6 Hz, C*H*OAc), 5.63 (1H, br s, NH); δ_C (125 MHz, $CDCl_3$) 21.0 (CH_3), 27.9 (CH_2), 31.0 (CH_2), 62.1 (CH), 79.6 (CH), 81.2 (CH), 158.6 (C), 170.5 (C); HRMS (ESI^+) found 208.0581, $C_8H_{11}NNaO_4$ (MNa^+) requires 208.0580.

4.26. *cis*- and *trans*-(2-Oxo-5-vinyloxazolidin-4-yl)methyl acetate (4p)

Colourless oil (42 mg, 46%) from carbamate **1**, obtained as an approximately 1:1 mixture of diastereoisomers. R_f 0.10 (petrol/ethyl acetate, 2:1); ν_{max} (thin film)/cm^{-1} 3300br m, 2959m, 1741s, 1393m, 1230m, 1044m; NMR data for *trans*-**4p**: δ_H (400 MHz, $CDCl_3$) 2.11 (3H, s, $COCH_3$), 3.80 (1H, dtd, *J* 5.9, 4.4, 1.0 Hz, C*H*NH), 4.07 (1H, dd, *J* 11.5, 5.9 Hz) and 4.25 (1H, dd, *J* 11.5, 4.4 Hz, CH_2OAc), 4.70–4.75 (1H, m, C*H*CH=), 5.36 (1H, app dt, *J* 10.5, 1.0 Hz) and 5.45 (1H, app dt, *J* 17.1, 1.0 Hz, =CH_2), 5.92 (1H, ddd, *J* 17.1, 10.5, 6.7 Hz, C*H*=CH_2), 6.31 (1H, br s, NH); δ_C (400 MHz, $CDCl_3$) 20.6 (CH_3), 56.8 (CH), 64.2 (CH_2), 79.3 (CH), 119.5 (CH_2), 133.6 (CH), 158.7 (C), 170.7 (C); NMR data for *cis*-**4p**: δ_H (400 MHz, $CDCl_3$) 2.10 (3H, s, $COCH_3$), 3.95 (1H, dd, *J* 11.4, 7.5 Hz) and 4.21 (1H, dd, *J* 11.4, 3.9 Hz, CH_2OAc), 4.10 (1H, app td, *J* 7.5, 3.9 Hz, C*H*NH), 5.12–5.18 (1H, m, C*H*CH=), 5.44 (1H, app dt, *J* 10.4, 1.0 Hz) and 5.45 (1H, app dt, *J* 17.2, 1.0 Hz, =CH_2), 5.89 (1H, ddd, *J* 17.2, 10.4, 6.7 Hz, C*H*=CH_2), 6.14 (1H, br s, NH); δ_C (400 MHz, $CDCl_3$) 20.7 (CH_3), 54.2 (CH), 63.2 (CH_2), 78.6 (CH), 121.0 (CH_2), 129.7 (CH), 158.7 (C), 170.6 (C); HRMS (ESI^+) found 208.0576, $C_8H_{11}NNaO_4$ (MNa^+) requires 208.0580.

4.27. (*R**)-4-[(*R**)-1-Hydroxybutyl]oxazolidin-2-one (5)[1e]

To a solution of oxazolidinone **4g** (16.0 mg, 0.080 mmol) in aq THF (1:1, 4.0 mL) at rt was added NaOH (3.80 mg, 0.096 mmol) and the mixture was stirred for 4 h. The reaction mixture was then diluted with water (5.0 mL), extracted with dichloromethane (3×10 mL) and the extracts were dried over $MgSO_4$. Concentration in vacuo and purification by column chromatography (ethyl acetate) afforded a sample of the title compound as a pale yellow oil (2.0 mg, 16%). R_f 0.18 (ethyl acetate); δ_H (400 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.1 Hz, CH_3), 1.32–1.45 (3H, m, C*H*H′CH_2CH_3), 1.52–1.57 (1H, m, CH*H*′CH_2CH_3), 2.20 (1H, d, *J* 6.4 Hz, OH), 3.52–3.57 (1H, m, C*H*OH),

3.76–3.81 (1H, m, C*H*NH), 4.20 (1H, dd, *J* 8.8, 5.8 Hz) and 4.46 (1H, app t, *J* 8.8 Hz, OCH_2), 5.68 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 13.9 (CH_3), 18.6 (CH_2), 35.5 (CH_2), 57.0 (CH), 67.0 (CH_2), 72.8 (CH), 159.6 (C) [lit.[1e] 13.9, 18.7, 35.2, 57.4, 67.4, 72.7, 160.8].

4.28. (4*R**,5*R**)-4-Hydroxymethyl-5-propyloxazolidin-2-one (6)[19]

To a stirred solution of oxazolidinone **4g** (16.0 mg, 0.080 mmol) in aq THF (1:1, 4.0 mL) at RT was added LiOH (2.30 mg, 0.096 mmol). After 5 h, more LiOH (2.30 mg, 0.096 mmol) was added and stirring was continued for a further 18 h. The reaction mixture was then diluted with water (5.0 mL), extracted with dichloromethane (3×10 mL) and the extracts were dried over $MgSO_4$. Concentration in vacuo afforded the title compound as a pale yellow oil (6.0 mg, 48%). R_f 0.20 (ethyl acetate); ν_{max} (thin film)/ cm^{-1} 3300br, 2961m, 1733s, 1407m, 1260w, 1079m; δ_H (400 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.3 Hz, CH_3), 1.38–1.55 (2H, m, CH_2CH_3), 1.57–1.80 (2H, m, $CH_2CH_2CH_3$), 3.52–3.60 (2H, m, C*H*NH, C*H*H′OH), 3.68–3.73 (1H, m, CHH′OH), 4.35–4.40 (1H, m, OCH), 6.41 (1H, br s, NH); δ_C (100 MHz, $CDCl_3$) 13.7 (CH_3), 17.9 (CH_2), 36.9 (CH_2), 59.3 (CH), 63.6 (CH_2), 78.9 (CH), 160.0 (C); HRMS (ESI^+) found 182.0785, $C_7H_{13}NNaO_3$ (MNa^+) requires 182.0788.

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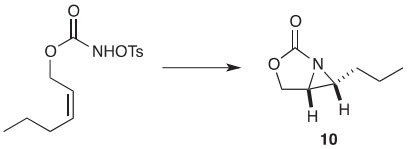
References and notes

1. (a) Donohoe, T. J.; Helliwell, M.; Johnson, P. D.; Keenan, M. *Chem. Commun.* **2001**, 2078–2079; (b) Donohoe, T. J.; Johnson, P. D.; Cowley, A.; Keenan, M. *J. Am. Chem. Soc.* **2002**, *124*, 12934–12935; (c) Donohoe, T. J.; Johnson, P. D.; Pye, R. J. *Org. Biomol. Chem.* **2003**, *1*, 2025–2028; (d) Donohoe, T. J.; Johnson, P. D.; Pye, R. J.; Keenan, M. *Org. Lett.* **2004**, *6*, 2583–2585; (e) Donohoe, T. J.; Chughtai, M. J.; Klauber, D. J.; Griffin, D.; Campbell, A. D. *J. Am. Chem. Soc.* **2006**, *128*, 2514–2515; (f) Donohoe, T. J.; Bataille, C. J. R.; Gattrell, W.; Kloesges, J.; Rossignol, E. *Org. Lett.* **2007**, *9*, 1725–1728; (g) Donohoe, T. J.; Callens, C. K. A.; Lacy, A. R.; Winter, C. *Eur. J. Org. Chem.* **2012**, 655–663.
2. (a) Feast, G. C.; Page, L. W.; Robertson, J. *Chem. Commun.* **2010**, *46*, 2835–2837 see also: (b) Stoll, A. H.; Blakey, S. B. *J. Am. Chem. Soc.* **2010**, *132*, 2108–2109.
3. (a) Robertson, J.; Feast, G. C.; White, L. V.; Steadman, V. A.; Claridge, T. D. W. *Org. Biomol. Chem.* **2010**, *8*, 3060–3063 see also: (b) Boralsky, L. A.; Marston, D.; Grigg, R. D.; Hershberger, J. C.; Schomaker, J. M. *Org. Lett.* **2011**, *13*, 1924–1927; (c) Grigg, R. D.; Schomaker, J. M.; Timokhin, V. *Tetrahedron* **2011**, *67*, 4318–4326; (d) Rigoli, J. W.; Boralsky, L. A.; Hershberger, J. C.; Marston, D.; Meis, A. R.; Guzei, I. A.; Schomaker, J. M. *J. Org. Chem.* **2012**, *77*, 2446–2455; (e) Weatherly, C. D.; Rigoli, J. W.; Schomaker, J. M. *Org. Lett.* **2012**, *14*, 1704–1707; (f) Rigoli, J. W.; Weatherly, C. D.; Alderson, J. M.; Vo, B. T.; Schomaker, J. M. *J. Am. Chem. Soc.* **2013**, *135*, 17238–17241; (g) Rigoli, J. W.; Weatherly, C. D.; Vo, B. T.; Neale, S.; Meis, A. R.; Schomaker, J. M. *Org. Lett.* **2013**, *15*, 290–293; (h) Weatherly, C. D.; Guzei, I. A.; Schomaker, J. M. *Eur. J. Org. Chem.* **2013**, 3667–3670; (i) Rigoli, J. W.; Guzei, I. A.; Schomaker, J. M. *Org. Lett.* **2014**, *16*, 1696–1699.
4. Kostiuk, S. L. *Chemistry Part II Thesis*, 2006 Oxford, UK.
5. Kocovsky, P. *Tetrahedron Lett.* **1986**, *27*, 5521–5524.
6. Robertson, J.; Abdulmalek, E. *Tetrahedron Lett.* **2009**, *50*, 3516–3518.
7. Cook, G. R.; Sun, L. *Org. Lett.* **2004**, *6*, 2481–2484.
8. Ibuka, T.; Suzuki, K.; Habashita, H.; Otaka, A.; Tamamura, H.; Mimura, N.; Miwa, Y.; Taga, T.; Fujii, N. *J. Chem. Soc., Chem. Commun.* **1994**, 2151–2152.
9. (a) Egli, M.; Dreiding, A. S. *Helv. Chim. Acta* **1986**, *69*, 1442–1460; (b) Rhouati, S.; Bernou, A. *J. Chem. Soc., Chem. Commun.* **1989**, 730–732; (c) Bergmeier, S. C.; Stanchina, D. M. *Tetrahedron Lett.* **1995**, *36*, 4533–4536; (d) Bergmeier, S. C.; Stanchina, D. M. *J. Org. Chem.* **1997**, *62*, 4449–4456; (e) Williams, D. R.; Rojas, C. M.; Bogen, S. L. *J. Org. Chem.* **1999**, *64*, 736–746; (f) Bergmeier, S. C.; Stanchina, D. M. *J. Org. Chem.* **1999**, *64*, 2852–2859; (g) Koohang, A.; Stanchina, C. L.; Coates, R. M. *Tetrahedron* **1999**, *55*, 9669–9686; (h) Kan, C.; Long, C. M.; Paul, M.; Ring, C. M.; Tully, S. E.; Rojas, C. M. *Org. Lett.* **2001**, *3*, 381–384; (i) Wu, P.-L.; Chung, T.-H.; Chou, Y. *J. Org. Chem.* **2001**, *66*, 6585–6594; (j) Mendlik, M. T.; Tao, P.; Hadad, C. M.; Coleman, R. S.; Lowary, T. L. *J. Org. Chem.* **2006**, *71*, 8059–8070; (k) Yoshimitsu, T.; Ino, T.; Tanaka, T. *Org. Lett.* **2008**, *10*, 5457–5460; (l) Orac, C. M.; Zhou, S.; Means, J. A.; Boehm, D.; Bergmeier, S. C.; Hines, J. V. *J. Med. Chem.* **2011**, *54*, 6786–6795.
10. (a) Duran, F.; Leman, L.; Ghini, A.; Burton, G.; Dauban, P.; Dodd, R. H. *Org. Lett.* **2002**, *4*, 2481–2483; (b) Guthikonda, K.; Du Bois, J. *J. Am. Chem. Soc.* **2002**, *124*, 13672–13673; (c) Wehn, P. M.; Lee, J.; Du Bois, J. *Org. Lett.* **2003**, *5*, 4823–4826; (d) Fruit, C.; Müller, P. *Tetrahedron: Asymmetry* **2004**, *15*, 1019–1026; (e) Wehn, P. M.; Du Bois, J. *Org. Lett.* **2005**, *7*, 4685–4688; (f) Duran, F. J.; Ghini, A. A.; Dauban, P.; Dodd, R. H.; Burton, G. *J. Org. Chem.* **2005**, *70*, 8613–8616; (g) Li, Z.; Ding, X.; He, C. *J. Org. Chem.* **2006**, *71*, 5876–5880; (h) Guthikonda, K.; Wehn, P. M.; Caliando, B. J.; Du Bois, J. *Tetrahedron* **2006**, *62*, 11331–11342; (i) Esteoule, A.; Duran, F.; Retailleau, P.; Dodd, R. H.; Dauban, P. *Synthesis* **2007**, 1251–1260; (j) Zalatan, D. N.; Du Bois, J. *J. Am. Chem. Soc.* **2008**, *130*, 9220–9221; (k) Ranatunga, S.; Del Valle, J. R. *Tetrahedron Lett.* **2009**, *50*, 2464–2466; (l) Wehn, P. M.; Du Bois, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 3802–3805; (m) Hoque, M. M.; Miyamoto, K.; Tada, N.; Shiro, M.; Ochiai, M. *Org. Lett.* **2011**, *13*, 5428–5431; (n) Malik, G.; Esteoule, A.; Retailleau, P.; Dauban, P. *J. Org. Chem.* **2011**, *76*, 7438–7448; (o) Cohen, D. T.; Eichman, C. C.; Phillips, E. M.; Zarefsky, E. R.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 7309–7313; (p) Valle, M. S.; Saraiva, M. F.; Retailleau, P.; de Almeida, M. V.; Dodd, R. H. *J. Org. Chem.* **2012**, *77*, 5592–5599.
11. (a) Levites-Agababa, E.; Menhaji, E.; Perlson, L. N.; Rojas, C. M. *Org. Lett.* **2002**, *4*, 863–865; (b) Padwa, A.; Stengel, T. *Org. Lett.* **2002**, *4*, 2137–2139; (c) Liang, J.-L.; Yuan, S.-X.; Chan, P. W. H.; Che, C.-M. *Tetrahedron Lett.* **2003**, *44*, 5917–5920; (d) Padwa, A.; Flick, A. C.; Leverett, C. A.; Stengel, T. *J. Org. Chem.* **2004**, *69*, 6377–6386; (e) Bodner, R.; Marcellino, B. K.; Severino, A.; Smenton, A. L.; Rojas, C. M. *J. Org. Chem.* **2005**, *70*, 3988–3996; (f) Hayes, C. J.; Beavis, P. W.; Humphries, L. A. *Chem. Commun.* **2006**, 4501–4502; (g) Knapp, S.; Yu, Y. *Org. Lett.* **2007**, *9*, 1359–1362; (h) Yamada, H.; Adachi, M.; Nishikawa, T. *Chem. Commun.* **2013**, *49*, 11221–11223.
12. For a recent overview see: Dequirez, G.; Pons, V.; Dauban, P. *Angew. Chem., Int. Ed.* **2012**, *51*, 7384–7395.
13. (a) Espino, C. G.; Du Bois, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 598–600; (b) Espino, C. G.; Wehn, P. M.; Chow, J.; Du Bois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935–6936.
14. (a) Sato, S.; Shibuya, M.; Kanoh, N.; Iwabuchi, Y. *Chem. Commun.* **2009**, 6264–6266; (b) Adams, C. S.; Boralsky, L. A.; Guzei, I. A.; Schomaker, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 10807–10810; (c) Zhang, Y.-Q.; Yuan, Y.-A.; Liu, G.-S.; Xu, H. *Org. Lett.* **2013**, *15*, 3910–3913.
15. Rh(II): (a) Lebel, H.; Huard, K.; Lectard, S. *J. Am. Chem. Soc.* **2005**, *127*, 14198–14199; (b) Huard, K.; Lebel, H. *Chem.—Eur. J.* **2008**, *14*, 6222–6230 Cu(II): (c) Lebel, H.; Lectard, S.; Parmentier, M. *Org. Lett.* **2007**, *9*, 4797–4800; (d) Liu, R.; Herron, S. R.; Fleming, S. A. *J. Org. Chem.* **2007**, *72*, 5587–5591 Fe(II): (e) Kamon, T.; Shigeoka, D.; Tanaka, T.; Yoshimitsu, T. *Org. Biomol. Chem.* **2012**, *10*, 2363–2365 No transition metal catalyst: (f) Deng, Q.-H.; Wang, J.-C.; Xu, Z.-J.; Zhou, C.-Y.; Che, C.-M. *Synthesis* **2011**, 2959–2967.
16. Liu, G.-S.; Zhang, Y.-Q.; Yuan, Y.-A.; Xu, H. *J. Am. Chem. Soc.* **2013**, *135*, 3343–3346.
17. Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769–3772.
18. (a) Neri, C.; Williams, J. M. J. *Tetrahedron: Asymmetry* **2002**, *13*, 2197–2199; (b) Neri, C.; Williams, J. M. J. *Adv. Synth. Catal.* **2003**, *345*, 835–848.
19. The (4*R*,5*S*)-isomer of 6 is known but no NMR data are provided for comparison: Schmidt, U.; Respondek, M.; Lieberknecht, A.; Werner, J.; Fischer. *Synthesis* **1989**, 256–261.
20. (a) Unsworth, W. P. *D.Phil. Thesis*, 2009 Oxford; (b) Clark, N. *Chemistry Part II Thesis*, 2011 Oxford; (c) Ronson, T. O. *Chemistry Part II Thesis*, 2011 Oxford.
21. For recent summaries: (a) Hansen, J.; Davies, H. M. L. *Coord. Chem. Rev.* **2008**, *252*, 545–555; (b) El-Deftar, M.; Adly, F. G.; Gardiner, M. G.; Ghanem, A. *Curr. Org. Chem.* **2012**, *16*, 1808–1836.
22. Preliminary studies with commercially available Rh_2(*S*-DOSP)$_4$ (2.5%) as catalyst (PhI(OAc)$_2$, MgO, pentane or benzene, 40–50 °C) gave low asymmetric induction, with ee values ranging from 0% (for **4g**) to 18% (for **4k**). Similar results were obtained with Rh_2(*S*-TBSP)$_4$ or Rh_2(*S*-MEOX)$_4$ as catalyst. More promising results were obtained using Lebel's procedure (Ref. 15a); for example, treatment of the *N*-*p*-toluenesulfonyloxy derivative of carbamate **3g** with Rh_2(*S*-MEOX)$_4$ as catalyst (K_2CO_3, acetone, rt) gave aziridine (−)-**10** (2% cat.: 59% yield, 28% ee; 5% cat.: 37% yield, 60% ee).



10
(the depicted absolute configuration is arbitrary)

In all cases, the ee was measured by NMR using the chiral shift reagent developed by Ema and Sakai: (a) Ema, T.; Tanida, D.; Sakai, T. *Org. Lett.* **2006**, *8*, 3773–3775; (b) Ema, T.; Tanida, D.; Sakai, T. *J. Am. Chem. Soc.* **2007**, *129*, 10591–10596.