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Tetrahedron
Tetrahedron 63 (2007) 10991–10999

Synthesis of enantiomerically pure tertiary 1,2-aminoalcohols by the highly diastereoselective reductive ring opening of oxazolidines

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Received 24 May 2007; revised 27 July 2007; accepted 16 August 2007
Available online 22 August 2007

Abstract—A number of enantiomerically pure 1,2-aminoalcohols containing tertiary nitrogen atoms bearing chiral substituents have been prepared by highly diastereoselective reductive ring cleavage of oxazolidines derived from ketones and pseudoephedrine or ephedrine. The ring cleavage occurs with retention of configuration.

1. Introduction

In connection with a number of projects in asymmetric catalysis, we required a range of non-racemic chiral 1,2-aminoalcohols, preferably containing tertiary nitrogen atoms bearing chiral substituents. We conjectured that such compounds could in principle be accessed by the reductive cleavage of oxazolidines prepared from ephedrine and pseudoephedrine (Fig. 1); indeed, 1,2-aminoalcohols and oxazolidines have both been widely used as ligand precursors and as chiral auxiliaries, and 1,2-aminoalcohols as peptide isosteres and as chiral building blocks.[1]

The synthesis of oxazolidines derived from aminoalcohols and aldehydes is well documented, but oxazolidines derived from ketones have only been reported infrequently, presumably as a result of the slow rate at which they are formed.[2]

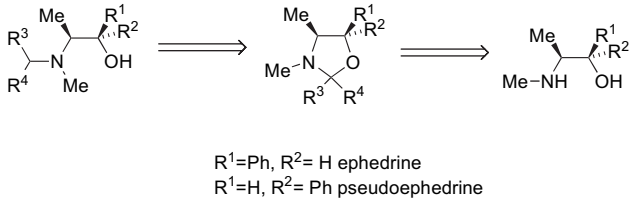

Figure 1. 1,2-Aminoalcohols from reductive cleavage of oxazolidines.

They are also easily hydrolyzed as a result of the additional stabilization of the incipient iminium ion in the ring-opened tautomer. Our initial attempts to prepare oxazolidines from mixtures of ketones and ephedrine or pseudoephedrine in dichloromethane solution at room temperature in the presence of 4 Å molecular sieve gave no oxazolidines after 2–3 days in the absence of any other catalyst. Experiments involving ketones such as acetophenone and 2-acetylfuran in reactions with ephedrine were equally unsuccessful when carried out using camphorsulfonic acid as catalyst in the presence of 4 Å molecular sieve, although a reaction between pseudoephedrine and isopropyl methyl ketone did proceed in dichloroethane at reflux in the presence of camphorsulfonic acid and 4 Å molecular sieve with poor diastereoselectivity (2:1); we have observed that pseudoephedrine is generally more reactive than ephedrine in these cyclocondensation reactions.

2. Discussion

We anticipated that use of a Lewis acid catalyst might meet with more success, and we have reported that scandium triflate in the presence of carefully dried 4 Å molecular sieve does indeed mediate the desired reaction.[3] Reactions of ketones with (1*S*,2*R*)-(−)-ephedrine or (1*S*,2*S*)-(+)-pseudoephedrine were initially carried out in dichloromethane (DCM) at room temperature or reflux, and later in 1,2-dichloroethane (DCE) at reflux, and were monitored by ^{1}H and ^{13}C NMR spectroscopies; the ^{13}C NMR chemical shift at position 2 in the oxazolidine products is observed at δ_C 96–99 ppm and is diagnostic. Table 1 shows a number of

Keywords: Stereoselective; Oxazolidine; Aminoalcohol; Enantiomerically pure; Reductive cleavage; Reduction.
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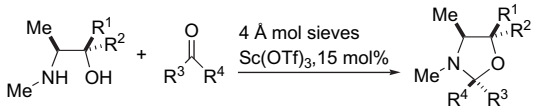
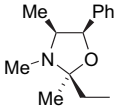
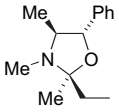
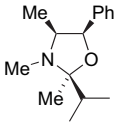
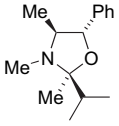
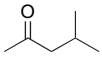
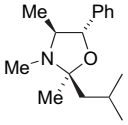
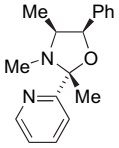
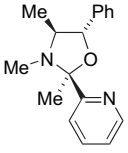
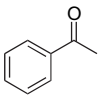
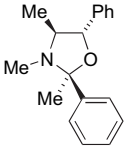
doi:10.1016/j.tet.2007.08.053

Table 1. Formation of oxazolidines **3–14** from (1*S*,2*R*)-(−)-ephedrine or (1*S*,2*S*)-(+)-pseudoephedrine using $Sc(OTf)_3$

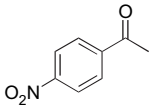
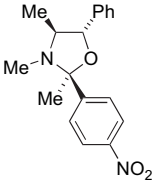
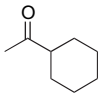
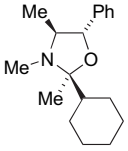
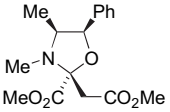
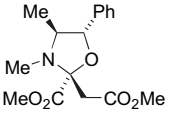


R^1=Ph, R^2= H ephedrine
R^1=H, R^2= Ph pseudoephedrine

Substrate	β-Aminoalcohol	Product[a,b]	Conditions	Yield (%) [d.r.]
	Ephedrine	 **4**	CH_2Cl_2, rt, 5 d DCE, Δ, 12 h	92 [2:1] 94 [2:1]
	Pseudoephedrine	 **5**	CH_2Cl_2, rt, 3 d DCE, Δ, 12 h	87 [4.5:1] 88 [5.7:1]
	Ephedrine	 **6**	CH_2Cl_2, rt, 14 d DCE, Δ, 7 d	81 [4:1] 95 [≥97:1][c]
	Pseudoephedrine	 **3**	CH_2Cl_2, rt, 7 d DCE, Δ, 2 d	99 [≥97.5:1][c] 96 [≥97.5:1][c]
	Pseudoephedrine	 **7**	DCE, Δ, 2 d	93 [6:1]
	Ephedrine	 **8**	CH_2Cl_2, rt, 7 d DCE, Δ, 3 d	61 [1.5:1] 72 [1.75:1]
	Pseudoephedrine	 **9**	CH_2Cl_2, rt, 9 d DCE, Δ, 3 d	68 [7.6:1] 64 [8.5:1]
	Ephedrine	—	CH_2Cl_2, rt, 14 d DCE, Δ, 8 d	NR NR
	Pseudoephedrine	 **10**	CH_2Cl_2, rt, 1 month DCE, Δ, 1 week	46 [7.5:1] 55 [≥97.5:1][c]

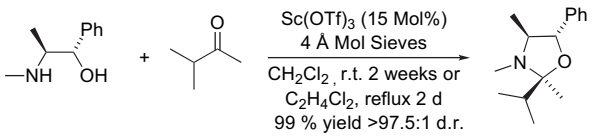
(*continued*)

Table 1. (*continued*)

Substrate	β-Aminoalcohol	Product[a,b]	Conditions	Yield (%) [d.r.]
	Pseudoephedrine	 **11**	DCE, Δ, 2 d	89 [≥97.5:1][c]
	Pseudoephedrine	 **12**	DCE, Δ, 2 d	94 [≥97.5:1][c]
	Ephedrine	 **13**	MeCN, Δ, 12 h	89 [97.5:1][c,d]
	Pseudoephedrine	 **14**	MeCN, Δ, 12 h	93 [97.5:1][c,d]

[a] Major diastereoisomer shown for clarity.
[b] Major diastereoisomer determined by NOE analysis.
[c] Only one diastereoisomer detected by 400 MHz ^{1}H NMR spectroscopy.
[d] Major diastereoisomer confirmed by X-ray crystallography and in agreement with NOE analysis.[3]

new examples together with our previously reported results to provide a context. For example, when (1*S*,2*S*)-(+)-pseudoephedrine **1** was treated with isopropyl methyl ketone **2** (1.0 equiv), scandium triflate (10 mol %) and molecular sieve, the oxazolidine **3** was formed in almost quantitative yield, and only one diastereoisomer could be detected by ^{1}H NMR spectroscopy (Scheme 1); the stereochemistry was determined by NOE analysis.

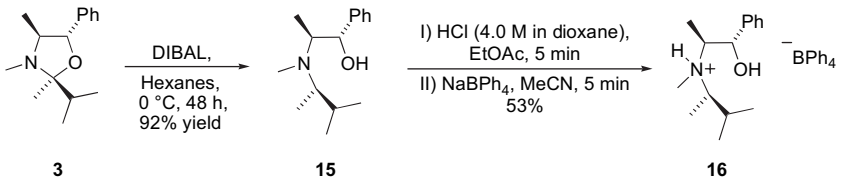


1 **2** **3**

Scheme 1.

The reactions were very clean, only oxazolidine products being visible in the ^{1}H and ^{13}C NMR spectra at 400 MHz; products were isolated after stirring the reaction mixtures with anhydrous sodium hydrogen carbonate in order to remove adventitious protic acid and the Lewis acid. Attempts to purify the products further by chromatography or recrystallization resulted in decomposition. One experiment was carried out using (1*S*,2*S*)-(+)-pseudoephedrine and butanone using indium(III) chloride but, although the yield of the products was similar (84%), the ratio of diastereoisomers was poor (1.2:1). Of particular interest is the observation that reactions carried out in 1,2-dichloroethane at reflux are generally more stereoselective than those carried out in dichloromethane.

We have also previously shown that the reductive cleavage of a number of different oxazolidines can be carried out using chlorotrimethylsilane in the presence of sodium cyanoborohydride.[4] This method, however, failed in our hands when 2,2-dialkyl oxazolidines derived from ketones were used as substrates. A number of alternative potential reducing agents were considered, including polymethyl hydrosiloxane[5] and chlorodibutyltin hydride–HMPA complex.[6] We also noted that reductive cleavage of the C–N bond in cyclic amidines has been reported using DIBAL.[7] Further, oxazolines have been reductively cleaved to yield carbinols by treatment with diborane in tetrahydrofuran[8] and by treatment with chloromethyl methyl ether followed by reaction with DIBAL.[9] In addition, 2-aryl-4,4-dimethyl-2-oxazolines and *trans*-(4*S*,5*S*)-2-aryl-(4-methoxymethyl)-5-phenyl-2-oxazolines give the corresponding aminoalcohols when treated with DIBAL.[10] A few examples of the reductive ring cleavage of oxazolidines by DIBAL have previously been reported.[2e,f] We therefore focused our attention on the use of DIBAL. Although, presumably due to reduced reactivity, DIBAL in tetrahydrofuran did not effect the reductive cleavage of (2*S*,4*S*,5*S*)-2-isopropyl-5-phenyl-2,3,4-trimethyloxazolidine **3**, we were pleased to observe that the corresponding 2-aminoethanol derivative **15** was produced with very high diastereoselectivity and in high yield



3 15 16

Scheme 2.

when the oxazolidine was treated with 1.5–2 equiv of DIBAL in hexanes (Scheme 2). Treatment of **15** with HCl followed by addition of sodium tetraphenylborate afforded the corresponding ammonium salt **16**, X-ray crystallographic analysis of which showed product **15** to have the absolute configuration *N*-methyl-*N*-((2*R*)-2-(3-methylbutyl))-(1*S*,2*S*)-1-phenyl-2-aminopropanol (Fig. 2), confirming retention of configuration in the ring cleavage process.

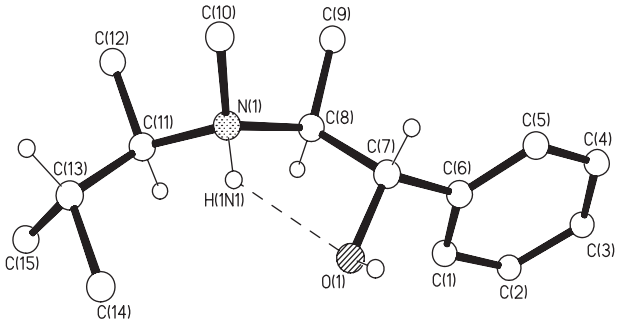
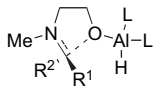


Figure 2. X-ray crystal structure of the cation in **16**.

Following this, a range of oxazolidines were similarly treated, providing the corresponding aminoalcohols **17**–**24** with high diastereoselectivities and yields (Table 2). Reaction of **9** resulted only in decomposition of the starting material. In all cases but one (**22**), the diastereoisomeric ratios of the oxazolidine starting materials were mirrored by the diastereoisomeric ratios of the derived aminoalcohols, suggesting a ring-opening process involving a high degree of stereoconservation. The absolute configuration of **20** was also determined by X-ray crystallography (Fig. 3). Interestingly, we were able to isolate oxazolidine **23** from reduction of diester **14** when using 4 equiv of DIBAL in hexanes. In order to achieve the products **22** and **24** of reductive cleavage of **13** and **14**, respectively, 6 equiv of DIBAL in hexanes were required.

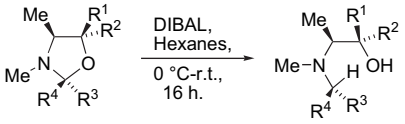
This level of retention of stereochemistry in a ring-opening reaction that formally proceeds through an acyclic iminium ion is remarkable and strongly suggests intramolecular hydride delivery through an intermediate position as shown in **25**, wherein the C–O bond is lengthened and weakened, but in which the oxazolidine ring remains intact.

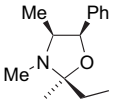
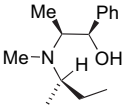
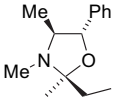
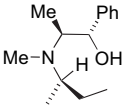
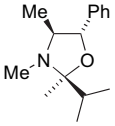
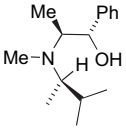
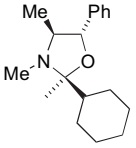
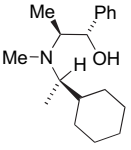
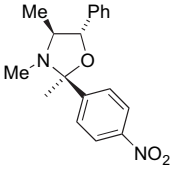
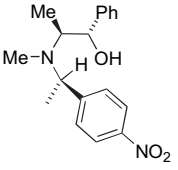
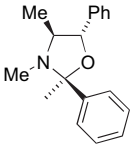
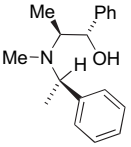
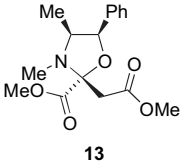
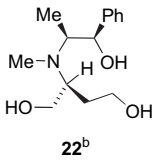


25

We have noted, however, that in our process, 1.5–2 equiv of DIBAL are normally required in order to ensure high yields and high selectivities (e.g., Scheme 3). This may suggest that

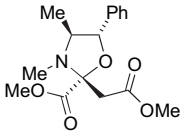
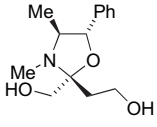
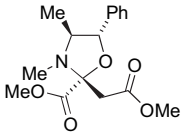
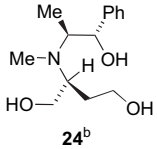
Table 2. Ring opening of oxazolidines using DIBAL



Oxazolidine	d.r.	Product[a]	d.r.	Yield (%)
 **4**	2:1	 **17**[b]	1.5:1	88
 **5**	4.5:1	 **18**[b]	4:1	91
 **3**	≥97.5:1	 **15**[d]	≥97.5:1[c]	92
 **12**	≥97.5:1	 **19**[b]	≥97.5:1[c]	87
 **11**	≥97.5:1	 **20**[d]	≥97.5:1[c]	91
 **10**	≥97.5:1	 **21**[b]	≥97.5:1[c]	78
 **13**	≥97.5:1	 **22**[b]	3:1[e]	75

(*continued*)

Table 2. (*continued*)

Oxazolidine	d.r.	Product[a]	d.r.	Yield (%)
 **14**	≥97.5:1	 **23**[b]	≥97.5:1[c,f]	63
 **15**	≥97.5:1	 **24**[b]	≥97.5:1[c,e]	80

[a] Major diastereoisomer shown for clarity.
[b] Major diastereoisomer assigned by analogy with known structures **15** and **20** and correlation of NMR data.
[c] Only one diastereoisomer detected by 400 MHz ^{1}H NMR spectroscopy.
[d] Major diastereoisomer confirmed by X-ray crystallography.
[e] Six equivalents of DIBAL used.
[f] Four equivalents of DIBAL used.

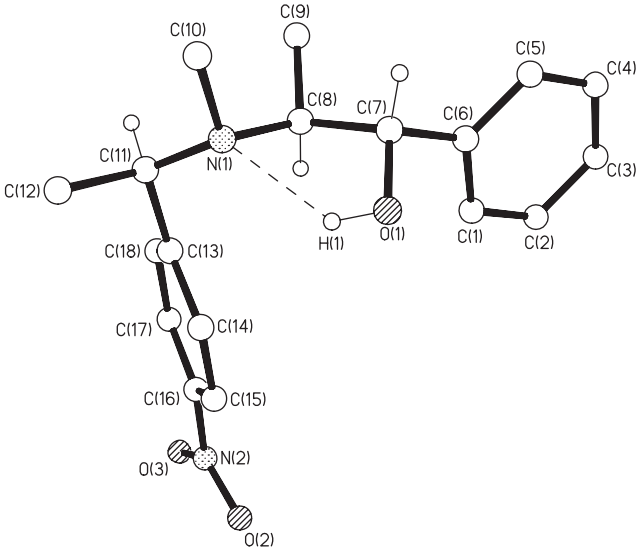
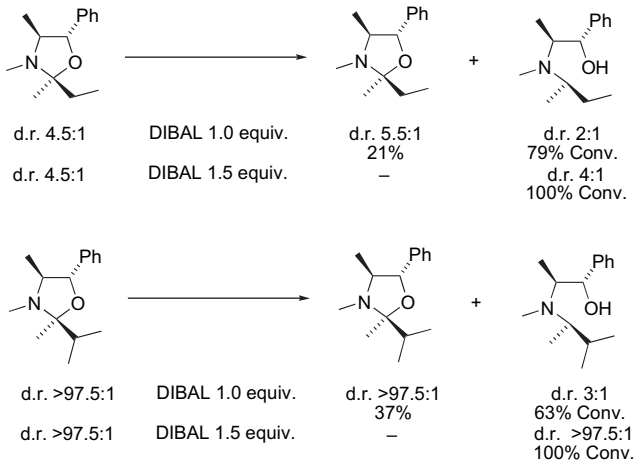


Figure 3. X-ray crystal structure of **20**.



Scheme 3.

some interaction between two molecules of DIBAL occurs during the reaction, and in this regard it may be significant that DIBAL in THF, a strongly chelating solvent, is ineffective. Husson has noted that in the ring-opening addition of alkynyl aluminium species to oxazolidines, 2 equiv of the aluminium reagent are required (addition of 1 equiv afforded not more than 50% yield of the ring-cleaved product).[11]

Other mechanistic possibilities, such as those involving C–O bond cleavage or intermolecular hydride delivery, would not account for the observed stereocontrol. The reasons for the poor stereocontrol in the ephedrine-derived examples remain unclear, but it perhaps results from an increased propensity for oxazolidine ring cleavage in these cases, conceivably resulting from steric interaction between the oxazolidine ring substituents.

3. Conclusion

DIBAL in hexanes has been shown to provide a very high degree of retention of configuration in reductive ring opening of 2,2-disubstituted oxazolidines derived from ketones and pseudoephedrine, perhaps resulting from intramolecular hydride delivery in an intermediate with a weakened but not broken C–O bond. Reductive ring opening of 2,2-disubstituted oxazolidines derived from ketones and ephedrine is less stereoselective.

4. Experimental procedures

4.1. General experimental methods

All infrared spectra were obtained using a Perkin–Elmer Paragon 1000 FTIR spectrophotometer; thin film spectra were acquired using sodium chloride plates. All ^{1}H and ^{13}C NMR spectra were obtained at 250.13 and 62.86 MHz, respectively, with a Bruker AC 250 MHz spectrometer, or at 400.13 and 100.62 MHz, respectively, with a Bruker DPX 400/Avance 400 MHz spectrometer, in deuteriochloroform solution unless otherwise stated, using TMS (tetramethylsilane) as the internal reference. Mass spectra were recorded using a Jeol-SX102 instrument utilizing electron-impact (EI) or fast atom bombardment (FAB) and by the EPSRC National Mass Spectrometry Service Centre at the University of Wales, Swansea, utilizing electrospray (ES). Analysis by GC–MS utilized a Fisons GC 8000 series (AS 800), with a 15 m×0.25 mm DB-5 column and an electron-impact low-resolution mass spectrometer. Melting points were recorded using an Electrothermal-IA 9100 melting point instrument and are uncorrected. Optical rotation values were measured with an Optical Activity-polAAar 2001 instrument operating at λ=589 nm, corresponding to the sodium D line, at the temperatures indicated. Microanalyses were performed on a Perkin–Elmer 2400 CHN Elemental Analyzer. All chromatographic manipulations used silica gel as the adsorbent. Reactions were monitored using thin layer chromatography (TLC) on aluminium-backed plates coated with Merck Kieselgel 60 F254 silica gel. TLC plates were visualized by UV radiation at a wavelength of 254 nm, or stained by exposure to an ethanolic solution of phosphomolybdic acid (acidified with concentrated sulfuric acid),

followed by charring where appropriate. Reactions requiring anhydrous conditions were carried out using flame-dried glassware under a nitrogen atmosphere unless otherwise stated. Reaction solvents were used as obtained commercially unless otherwise stated. Light petroleum (bp 40–60 °C) was distilled from calcium chloride prior to use. Ethyl acetate was distilled over calcium sulfate or chloride. Dichloromethane was distilled over calcium hydride. Dichloroethane was used as purchased.

4.1.1. Representative procedures for the formation of oxazolidines from aminoalcohols and ketones.

4.1.1.1. (+)-(2*S*,4*S*,5*S*)-2-Isopropyl-2,3,4-trimethyl-5-phenyloxazolidine (3). Pseudoephedrine (0.50 g, 3.0 mmol), scandium triflate (0.22 g, 0.5 mmol) and 3-methylbutanone (0.26 g, 3.0 mmol) were added to a suspension of flame-dried 4 Å molecular sieve (2.20 g) in dichloroethane (7.0 mL). The mixture was heated under reflux for 48 h, allowed to cool to room temperature, solid sodium hydrogen carbonate (1.0 g) added and stirring continued for a further 2 h at room temperature. The mixture was filtered, the filtrate washed with water (2×5 mL) and the organic layer dried over anhydrous magnesium sulfate. Solvents were removed under reduced pressure to afford a colourless oil (0.67 g, 96%); $[\alpha]_D^{25}$ +39.0 (*c* 1.00, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3130, 2924, 2761, 1459, 1373, 1326, 1189, 1135; δ_H (250 MHz; $CDCl_3$) 0.95 (3H, d, *J* 2.8 Hz), 0.98 (3H, d, *J* 2.8 Hz), 1.01 (3H, d, *J* 6.0 Hz), 1.25 (3H, s), 1.70–1.86 (1H, m), 2.20 (3H, s) 2.41–2.50 (1H, m), 4.30 (1H, d, *J* 8.9 Hz), 7.22–7.40 (5H, m); δ_C (100 MHz; $CDCl_3$) 7.7, 14.4, 14.6, 18.6, 33.7, 36.4, 65.1, 85.4, 98.6, 126.2, 127.0, 127.7, 140.4; *m/z* (FAB) 234.1855; $C_{15}H_{24}NO$ (MH^+) requires: 234.1858.

4.1.1.2. (2*R*,4*S*,5*R*)- and (2*S*,4*S*,5*R*)-2,3,4-Trimethyl-2-ethyl-5-phenyloxazolidine (4). Prepared according to the representative procedure from ephedrine (3.0 g, 18.8 mmol) and 2-butanone (1.97 g, 27.3 mmol). Colourless oil (3.74 g, 92%); ν_{max} (neat)/cm^{-1} 3317, 2970, 2931, 1458, 1373, 1320, 1203, 1134, 1049; δ_H (400 MHz; $CDCl_3$) (2:1 mixture of diastereoisomers) 0.63 (3H, d, *J* 6.4 Hz, major and minor), 1.01 (3H, t, *J* 7.5 Hz, minor), 1.07 (3H, t, *J* 7.5 Hz, major), 1.17 (3H, s, major), 1.44 (3H, s, minor), 1.74–1.85 (2H, m, major and 2H, m, minor), 2.23 (3H, s, major), 2.30 (3H, s, minor), 3.18 (1H, dq, *J* 6.4, 8.0 Hz, major), 3.22 (1H, dq, *J* 6.4, 8.0 Hz, minor), 5.02 (1H, d, *J* 8.0 Hz, minor), 5.05 (1H, d, *J* 8.0 Hz, major), 7.22–7.34 (5H, m, major and 5H, m, minor); δ_C (100 MHz; $CDCl_3$) (major diastereoisomer) 8.4, 15.9, 32.1, 33.0, 33.7, 60.6, 80.3, 96.6, 125.9, 127.4, 127.8, 140.4; *m/z* (FAB) 220.1698; $C_{14}H_{22}NO$ (MH^+) requires: 220.1701.

4.1.1.3. (2*R*,4*S*,5*S*)- and (2*S*,4*S*,5*S*)-2,3,4-Trimethyl-2-ethyl-5-phenyloxazolidine (5). Prepared according to the representative procedure from pseudoephedrine (3.0 g, 18.8 mmol) and 2-butanone (1.97 g, 27.3 mmol). Colourless oil (3.6 g, 88%); ν_{max} (neat)/cm^{-1} 3827, 3812, 2870, 2787, 1493, 1454, 1370, 1166; δ_H (400 MHz; $CDCl_3$) (5.7:1 mixture of diastereoisomers) 0.97 (3H, t, *J* 7.6 Hz, major), 1.05 (3H, d, *J* 6.0 Hz, major), 1.06 (3H, d, *J* 6.0 Hz, minor), 1.11 (3H, t, *J* 7.6 Hz, minor), 1.28 (3H, s, major), 1.36 (3H, s, minor), 1.50–1.75 (2H, m, major and 2H, m, minor), 2.24 (3H, s, major), 2.32 (3H, s, minor), 2.51–2.58 (1H, m, major), 2.60–2.64 (1H, m, minor), 4.37 (1H, d, *J* 8.8 Hz, major), 4.44 (1H, d, *J* 8.8 Hz, minor), 7.20–7.40 (5H, m, major and 5H, m, minor); δ_C (100 MHz; $CDCl_3$) (major diastereoisomer) 7.7, 14.6, 20.5, 32.5, 32.7, 65.2, 85.7, 97.0, 126.8, 127.8, 128.3, 140.3; *m/z* (FAB) 219.1625; $C_{14}H_{21}NO$ (M^+) requires: 219.1623.

4.1.1.4. (−)-(2*S*,4*S*,5*R*)-2,3,4-Trimethyl-2-(1-methylethyl)-5-phenyloxazolidine (6). Prepared according to the representative procedure from ephedrine (3.0 g, 18.8 mmol) and 3-methyl-butanone (1.34 g, 27.3 mmol). Colourless oil (3.43 g, 81%); $[\alpha]_D^{25}$ −6.1 (*c* 1.04, $CHCl_3$); ν_{max} (neat)/cm^{-1} 4299, 3736, 3261, 2929, 2362, 1460, 1375, 1336, 1198, 1146; δ_H (400 MHz; $CDCl_3$) 0.61 (3H, d, *J* 6.4 Hz), 1.08 (3H, d, *J* 6.9 Hz), 1.09 (3H, d, *J* 6.9 Hz), 1.20 (3H, s), 1.85–1.92 (1H, m), 2.24 (3H, s), 3.07–3.14 (1H, m), 5.05 (1H, d, *J* 8.4 Hz), 7.25–7.45 (5H, m); δ_C (100 MHz; $CDCl_3$) 8.7, 14.6, 18.2, 32.5, 34.0, 60.1, 80.7, 97.0, 126.5, 127.5, 129.6, 140.6; *m/z* (FAB) 234.1858; $C_{15}H_{24}NO$ (MH^+) requires: 234.1858.

4.1.1.5. (2*R*,4*S*,5*S*)- and (2*S*,4*S*,5*S*)-2-Isobutyl-2,3,4-trimethyl-5-phenyloxazolidine (7). Prepared according to the representative procedure from pseudoephedrine (0.50 g, 3.0 mmol) and 4-methyl-2-pentanone (0.45 g, 4.5 mmol). Colourless oil (0.69 g, 93%); ν_{max} (neat)/cm^{-1} 3125, 2926, 2764, 1460, 1373, 1190, 1135; δ_H (400 MHz; $CDCl_3$) (major diastereoisomer) 0.95 (3H, d, *J* 6.7 Hz), 0.99 (3H, d, *J* 6.7 Hz), 1.07 (3H, d, *J* 6.0 Hz), 1.27 (3H, s), 1.50 (1H, dd, *J* 6.6, 14.6 Hz), 1.60 (1H, dd, *J* 6.6, 14.6 Hz), 1.91–1.97 (1H, m), 2.23 (3H, s), 2.51–2.55 (1H, m), 4.39 (1H, d, *J* 8.8 Hz), 7.26–7.37 (5H, m); δ_C (100 MHz; $CDCl_3$) (major diastereoisomer) 14.7, 21.1, 23.6, 24.3, 24.7, 32.5, 47.8, 64.7, 85.5, 97.3, 126.7, 127.8, 128.3, 140.5; *m/z* (FAB) 248.2017; $C_{16}H_{26}NO$ (MH^+) requires: 248.2014.

4.1.1.6. (2*R*,4*S*,5*R*)- and (2*S*,4*S*,5*R*)-2-(2-Pyridyl)-2,3,4-trimethyl-5-phenyloxazolidine (8). Prepared according to the representative procedure from ephedrine (0.50 g, 3.0 mmol) and 2-acetylpyridine (0.55 g, 4.5 mmol). Colourless oil (0.58 g, 72%); ν_{max} (neat)/cm^{-1} 3294, 3085, 1585, 1493, 1454, 1358, 1327, 1238, 1196, 1136; δ_H (250 MHz; $CDCl_3$) (major diastereoisomer) 0.98 (3H, d, *J* 4.9 Hz), 1.32 (3H, s), 2.63 (3H, s), 2.65–2.66 (1H, m), 5.22 (1H, d, *J* 4.8 Hz), 7.25–7.91 (8H, m), 8.52–8.53 (1H, m); δ_C (100 MHz; $CDCl_3$) (major diastereoisomer) 24.9, 33.9, 60.2, 76.9, 82.1, 97.3, 121.2, 127.9, 128.1, 128.4, 136.2, 137.0, 140.7, 148.8, 163.0; *m/z* (FAB) 268.1573; $C_{17}H_{20}N_2O$ (M^+) requires: 268.1577.

4.1.1.7. (2*R*,4*S*,5*S*)- and (2*S*,4*S*,5*S*)-2-(2-Pyridyl)-2,3,4-trimethyl-5-phenyloxazolidine (9). Prepared according to the representative procedure from pseudoephedrine (0.50 g, 3.0 mmol) and 2-acetylpyridine (0.55 g, 4.5 mmol). Colourless oil (0.51 g, 64%); ν_{max} (neat)/cm^{-1} 4350, 3482, 3679, 1304, 1491, 1437, 1356, 1200, 1135, 1126; δ_H (400 MHz; $CDCl_3$) (major diastereoisomer) 1.13 (3H, d, *J* 5.6 Hz), 1.80 (3H, s), 2.45 (3H, s), 2.73–2.67 (1H, m), 4.64 (1H, d, *J* 8.8 Hz), 7.19–7.45 (5H, m) 7.60–7.78 (3H, m), 8.50–8.63 (1H, m); δ_C (100 MHz; $CDCl_3$) (major diastereoisomer) 14.5, 19.3, 32.8, 65.9, 86.0, 96.8, 119.6, 122.4, 126.7, 127.9, 128.3, 136.6, 139.5, 148.1, 163.9; *m/z* (FAB) 269.1656; $C_{17}H_{21}N_2O$ (MH^+) requires: 269.1654.

4.1.1.8. (+)-(2*S*,4*S*,5*S*)-2,3,4-Trimethyl-2,5-diphenyloxazolidine (10). Prepared according to the representative procedure from pseudoephedrine (0.50 g, 3.0 mmol) and acetophenone (0.60 g, 4.5 mmol). Colourless oil (0.44 g, 55%); $[\alpha]_D^{25}$ +67.0 (*c* 1.11, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3488, 2309, 1483, 1437, 1360, 1352, 1278, 1230, 1187, 1121; δ_H (400 MHz; $CDCl_3$) 1.14 (3H, d, *J* 6.0 Hz), 1.72 (3H, s), 2.36 (3H, s), 2.70–2.80 (1H, m), 4.52 (1H, d, *J* 8.7 Hz), 7.30–7.67 (10H, m); δ_C (100 MHz; $CDCl_3$) 14.7, 20.7, 33.1, 65.8, 85.2, 96.2, 125.9, 126.5, 127.4, 127.7, 127.9, 139.5, 139.5, 145.3; *m/z* (FAB) 268.1702; $C_{18}H_{22}NO$ (MH^+) requires: 268.1701.

4.1.1.9. (+)-(2*S*,4*S*,5*S*)-2,3,4-Trimethyl-2-(4-nitrophenyl)-5-phenyloxazolidine (11). Prepared according to the representative procedure from pseudoephedrine (0.50 g, 3.0 mmol) and 4-nitroacetophenone (0.74 g, 4.5 mmol). Colourless oil (0.83 g, 89%); $[\alpha]_D^{25}$ +54.0 (*c* 1.10, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3061, 2970, 1604, 1523, 1445, 1355, 1043; δ_H (400 MHz; $CDCl_3$) 1.12 (3H, d, *J* 6.0 Hz), 2.41 (3H, s), 2.69 (3H, s), 2.70–2.81 (1H, m), 4.45 (1H, d, 8.8 Hz), 7.26–7.39 (5H, m), 7.83 (2H, d, *J* 9.0 Hz), 8.20 (2H, d, *J* 9 Hz); δ_C (100 MHz; $CDCl_3$) 15.1, 22.7, 33.8, 66.5, 85.5, 97.9, 123.2, 127.2, 127.7, 128.2, 129.3, 138.9, 147.4, 153.2; *m/z* (FAB) 313.1554; $C_{18}H_{21}N_2O_3$ (MH^+) requires: 313.1552.

4.1.1.10. (+)-(2*S*,4*S*,5*S*)-2-Cyclohexyl-2,3,4-trimethyl-5-phenyloxazolidine (12). Prepared according to the representative procedure from pseudoephedrine (0.50 g, 3.0 mmol) and cyclohexyl methyl ketone (0.57 g, 4.5 mmol). Colourless oil (0.77 g, 94%); $[\alpha]_D^{25}$ +37.0 (*c* 1.00, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3133, 2922, 2758, 1461, 1371, 1194, 1130; δ_H (400 MHz; $CDCl_3$) 0.95 (3H, d, *J* 5.6 Hz), 1.09–1.24 (6H, m), 1.50–1.85 (5H, m), 2.06 (3H, s), 2.16 (3H, s), 2.36–2.45 (1H, m), 4.24 (1H, d, 8.8 Hz), 7.20–7.27 (5H, m); δ_C (100 MHz; $CDCl_3$) 14.5, 18.7, 25.7, 25.9, 27.9, 28.4, 33.4, 65.7, 85.8, 98.4, 126.9, 128.3, 128.6, 140.3; *m/z* (FAB) 274.2161; $C_{18}H_{28}NO$ (MH^+) requires: 274.2171.

4.1.1.11. (−)-(2*R*,4*S*,5*R*)-2-(Methoxycarbonylmethyl)-2-(methoxycarbonyl)-3,4-dimethyl-5-phenyloxazolidine (13). Scandium triflate (0.22 g, 0.5 mmol) and but-2-ynedioic acid dimethyl ester (0.43 g, 3.0 mmol) were added to a solution of ephedrine (0.50 g, 3.0 mmol) in acetonitrile (10.0 mL). The mixture was heated under reflux for 24 h, allowed to cool to room temperature, solid sodium hydrogen carbonate (1.0 g) added and stirring continued for a further 2 h at room temperature. The solution was filtered, washed with water (2×5 mL) and the organic layer dried over anhydrous magnesium sulfate. Solvents were removed under reduced pressure to afford **13** as an orange oil; crystallization from methanol afforded colourless prisms (0.82 g, 89%). mp 71–73 °C (lit.,[12] 72 °C); $[\alpha]_D^{25}$ −27.6 (*c* 1.16, $CHCl_3$); ν_{max} (film)/cm^{-1} 3026, 2952, 1751, 1730, 1437, 1346, 1151, 1073; δ_H (250 MHz; $CDCl_3$) 0.61 (3H, d, *J* 6.4 Hz), 2.28 (3H, s) 2.83 (1H, d, *J* 16.1 Hz), 3.17–3.24 (1H, m), 3.43 (1H, d, *J* 16.1 Hz), 3.69 (3H, s), 3.82 (3H, s), 5.39 (1H, d, *J* 8.1 Hz) 7.20–7.45 (5H, m); δ_C (100 MHz; $CDCl_3$) 15.3, 33.5, 41.0, 51.8, 51.9, 60.0, 83.3, 95.3, 127.7, 127.8, 127.9, 139.3, 169.8, 170.1.

4.1.1.12. (−)-(2*R*,4*S*,5*S*)-2-(Methoxycarbonylmethyl)-2-(methoxycarbonyl)-3,4-dimethyl-5-phenyloxazolidine (14). Scandium triflate (0.22 g, 0.5 mmol) and but-2-ynedioic acid dimethyl ester (0.43 g, 3.0 mmol) were added to a solution of pseudoephedrine (0.50 g, 3.0 mmol) in acetonitrile (10 mL). The mixture was heated under reflux for 24 h, allowed to cool to room temperature, solid sodium hydrogen carbonate (1.0 g) added and stirring continued for a further 2 h at room temperature. The solution was filtered, washed with water (2×5 mL) and the organic layer dried over anhydrous magnesium sulfate. Solvents were removed under reduced pressure to afford an orange oil; crystallization from methanol afforded **14** as colourless prisms (0.86 g, 93%); mp 74–76 °C (lit.,[12] 76 °C); $[\alpha]_D^{25}$ −10.1 (*c* 1.19, $CHCl_3$); ν_{max} (film)/cm^{-1} 3030, 2952, 1751, 1730, 1457, 1346, 1202, 1152, 1074, 752, 701; δ_H (400 MHz; $CDCl_3$) 1.03 (3H, d, *J* 6.0 Hz), 2.29 (3H, s) 2.86–2.90 (1H, m), 2.87 (1H, d, *J* 16.0 Hz), 3.19 (1H, d, *J* 16.0 Hz), 3.69 (3H, s), 3.84 (3H, s), 4.53 (1H, d, *J* 8.8 Hz) 7.26–7.60 (5H, m); δ_C (100 MHz; $CDCl_3$) 14.1, 32.5, 41.3, 51.6, 51.7, 64.3, 87.1, 95.5, 127.6, 128.2, 128.6, 138.2, 170.1, 170.5; *m/z* (ESI) 308.1493; $C_{16}H_{22}NO_5$ (MH^+) requires: 308.1498.

4.1.1.13. (+)-*N*-Methyl-*N*-((2*R*)-2-(3-methylbutyl))-(1*S*,2*S*)-1-phenyl-2-aminopropanol *N*-H ammonium tetraphenylborate salt (16). (+)-*N*-Methyl-*N*-((2*R*)-2-(3-methylbutyl))-(1*S*,2*S*)-1-phenyl-2-aminopropanol **15** (0.72 g, 3.0 mmol) was dissolved in ethanol (10 mL) and HCl in dioxane (4.0 M, 0.77 mL) added dropwise. The mixture was stirred for 30 min and sodium tetraphenylborate (1.10 g, 3.2 mmol) added as a solution in acetonitrile (2 mL). The solvents were removed under reduced pressure to yield a colourless solid, which was suspended in ethanol, removed by filtration and washed successively with water, ethanol and diethyl ether, to give **16** as a colourless solid (0.90 g, 54%).

4.1.2. Representative procedures for the ring opening of oxazolidines with DIBAL.

4.1.2.1. (+)-*N*-Methyl-*N*-((2*R*)-2-(3-methylbutyl))-(1*S*,2*S*)-1-phenyl-2-aminopropanol (15). (2*S*,4*S*,5*S*)-2-Isopropyl-2,3,4-trimethyl-5-phenyloxazolidine **3** (1.00 g, 4.3 mmol) was dissolved in hexanes (30 mL) and the solution cooled using an ice bath. DIBAL in hexanes (6.4 mL, 6.4 mmol, 1.0 M, 1.5 equiv) was added dropwise over 10 min, the solution allowed to attain room temperature and stirring continued for 48 h. Ethyl acetate (30 mL) was added followed by a saturated solution of sodium potassium tartrate (20 mL) and the mixture stirred for a further 30 min. The layers were separated and the aqueous phase washed with ethyl acetate (3×30 mL), the combined organic layers dried ($MgSO_4$) and the solvents removed under reduced pressure to afford the crude product as a colourless oil. Column chromatography eluting with light petroleum/ethyl acetate (20:1) afforded product **15** as a colourless oil (0.92 g, 92%); $[\alpha]_D^{25}$ +86.0 (*c* 1.10, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3326, 3027, 2969, 2871, 2359, 1453, 1371, 1088, 1048, 1027, 765, 700; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, d, *J* 6.4 Hz), 0.93 (3H, d, *J* 6.8 Hz), 1.05 (6H, d, *J* 6.4 Hz), 1.73–1.82 (1H, m), 2.16 (3H, s), 2.37–2.44 (1H, m), 2.66–2.74 (1H, m), 4.18 (1H, d, *J* 9.2 Hz), 7.26–7.37 (5H, m); δ_C (100 MHz, $CDCl_3$) 11.3, 13.0, 19.7, 20.9, 32.0, 66.1, 66.5, 75.5, 127.5, 127.6, 128.2, 142.5; *m/z* (ESI) 236.2008; $C_{15}H_{26}NO$ (MH^+) requires: 236.2014.

4.1.2.2. *N*-Methyl-*N*-((2*R*)-2-butyl)-(1*R*,2*S*)-1-phenyl-2-aminopropanol (17)+enantiomer. Prepared according to the representative procedure from (2*R*,4*S*,5*R*)- and (2*S*,4*S*,5*R*)-2-ethyl-2,3,4-trimethyl-5-phenyloxazolidine **4** (2.00 g, 8.2 mmol). Colourless oil (1.77 g, 88%); ν_{max} (film)/cm^{-1} 3314, 3028, 2963, 2872, 2348, 1604, 1493, 1453, 1372, 1026, 994, 746, 700; δ_H (400 MHz; $CDCl_3$) (2:1 mixture of diastereoisomers) 0.71 (3H, d, *J* 6.8 Hz, minor), 0.76 (3H, d, *J* 6.8 Hz, major), 0.82–0.89 (3H, m, major and 6H, m, minor), 0.95 (3H, d, *J* 6.8 Hz, major), 1.23–1.33 (2H, m, major), 1.44–1.51 (2H, m, minor), 2.02 (3H, s, major), 2.18 (3H, s, minor), 2.72–2.78 (1H, m, major and 2H, m, minor), 2.86–2.89 (1H, m, major), 4.70 (1H, d, *J* 4.4 Hz, major), 4.83 (1H, d, *J* 3.5 Hz, minor), 7.13–7.25 (5H, m, major and 5H, m, minor); δ_C (100 MHz; $CDCl_3$) (major diastereoisomer) 11.6, 12.0, 14.6, 26.7, 30.2, 58.4, 61.5, 72.7, 126.1, 126.7, 127.9, 142.0 (minor diastereoisomer) 11.5, 11.7, 14.1, 27.3, 32.2, 56.3, 61.8, 72.1, 125.9, 126.7, 128.0, 142.1; *m*/*z* (FAB) 222.1861; $C_{14}H_{24}NO$ (MH^+) requires: 222.1858.

4.1.2.3. *N*-Methyl-*N*-((2*R*)-2-butyl)-(1*S*,2*S*)-1-phenyl-2-aminopropanol (18)+enantiomer. Prepared according to the representative procedure from (2*R*,4*S*,5*S*)- and (2*S*,4*S*,5*S*)-2-ethyl-2,3,4-trimethyl-5-phenyloxazolidine **5** (2.00 g, 9.1 mmol). Colourless oil (1.84 g, 91%); ν_{max} (film)/cm^{-1} 3314, 3028, 2966, 1604, 1493, 1453, 1371, 1218, 1048, 923, 762, 700; δ_H (400 MHz; $CDCl_3$) (4:1 mixture of diastereoisomers) 0.83 (3H, d, *J* 6.6 Hz, minor), 0.87 (3H, d, *J* 6.6 Hz, major), 0.91–0.93 (3H, m, minor), 0.93 (3H, t, *J* 7.6 Hz, major), 1.05 (3H, d, *J* 6.3 Hz, minor), 1.06 (3H, d, *J* 6.5 Hz, major), 1.29–1.36 (1H, m, major), 1.37–1.52 (1H, m, minor), 1.58–1.68 (1H, m, major and 1H, m, minor), 2.18 (3H, s, major), 2.29 (3H, s, minor), 2.69–2.73 (2H, m, major and 2H, m, minor), 4.12 (1H, d, *J* 9.2 Hz, minor), 4.14 (1H, d, *J* 9.6 Hz, major), 7.26–7.37 (5H, m, major and 5H, m, minor); δ_C (100 MHz; $CDCl_3$) (major diastereoisomer) 11.5, 11.6, 16.5, 27.7, 27.8, 61.6, 64.2, 75.0, 127.4, 127.6, 128.2, 142.6; (minor diastereoisomer) 11.3, 11.4, 16.5, 27.8, 32.0, 59.9, 61.0, 74.6, 127.4, 127.6, 128.2, 142.7; *m*/*z* (FAB) 222.1861; $C_{14}H_{24}NO$ (MH^+) requires: 222.1858.

4.1.2.4. (+)-*N*-Methyl-*N*-((1*R*)-1-(1-cyclohexylethyl))-(1*S*,2*S*)-1-phenyl-2-aminopropanol (19). Prepared according to the representative procedure from (+)-(2*S*,4*S*,5*S*)-cyclohexyl-2,3,4-trimethyl-5-phenyloxazolidine **12** (1.0 g, 3.7 mmol). Colourless oil (0.88 g, 87%); $[\alpha]_D^{25}$ +40.7 (*c* 1.13, $CHCl_3$); ν_{max} (film)/cm^{-1} 3337, 3060, 2923, 2851, 2360, 1604, 1450, 1372, 1341, 1198, 1087, 1047, 770, 700; δ_H (400 MHz; $CDCl_3$) 0.89 (3H, d, *J* 6.6 Hz), 0.92–1.09 (1H, m), 1.06 (3H, d, *J* 6.6 Hz), 1.10–1.30 (4H, m), 1.39–1.47 (1H, m), 1.65–1.70 (1H, m), 1.76–1.82 (3H, m), 1.98–2.02 (1H, m), 2.16 (3H, s), 2.47 (1H, quint, *J* 7.6 Hz), 2.68–2.72 (1H, m), 4.20 (1H, d, *J* 9.4 Hz), 7.26–7.37 (5H, m); δ_C (100 MHz; $CDCl_3$) 11.6, 13.1, 26.4, 26.9, 30.1, 30.8, 41.6, 65.9, 66.5, 75.5, 127.4, 127.6, 128.2, 142.4; *m*/*z* (ESI) 276.2323; $C_{18}H_{30}NO$ (MH^+) requires: 276.2327.

4.1.2.5. (+)-*N*-Methyl-*N*-((1*R*)-1-(1-(4-nitrophenyl)-ethyl))-(1*S*,2*S*)-1-phenyl-2-aminopropanol (20). Prepared according to the representative procedure from (+)-(2*S*,4*S*,5*S*)-2,3,4-trimethyl-2-(4-nitrophenyl)-5-phenyloxazolidine **11** (1.0 g, 3.2 mmol). Recrystallized from hexane, pale yellow crystals (0.91 g, 91%); mp 144–147 °C; $[\alpha]_D^{25}$ +47.5 (*c* 0.52, $CHCl_3$); $C_{18}H_{22}N_2O_3$: calcd C 68.77, H 7.05, N 8.91; found C 68.85, H 6.98, N 8.79; ν_{max} (film)/cm^{-1} 3350, 3060, 2971, 2359, 1604, 1520, 1455, 1345, 1042, 856, 756, 701; δ_H (400 MHz; $CDCl_3$) 0.68 (3H, d, *J* 6.6 Hz), 1.48 (3H, d, *J* 8.0 Hz), 2.36 (3H, s), 2.53–2.60 (1H, m), 3.83 (1H, q, *J* 6.6 Hz), 4.23 (1H, d, *J* 9.6 Hz), 4.90 (1H, br s), 7.09–7.26 (5H, m), 7.51 (2H, d, *J* 8.9 Hz), 8.24 (2H, d, *J* 8.9 Hz); δ_C (100 MHz; $CDCl_3$) 7.8, 21.4, 31.2, 61.7, 61.9, 74.7, 124.0, 127.2, 127.8, 128.2, 141.7, 147.2, 152.1; *m*/*z* (ESI) 315.1702; $C_{18}H_{23}N_2O_3$ (MH^+) requires: 315.1709.

4.1.2.6. (+)-*N*-Methyl-*N*-((1*R*)-1-(1-phenylethyl))-(1*S*,2*S*)-1-phenyl-2-aminopropanol (21). Prepared according to the representative procedure from (+)-(2*S*,4*S*,5*S*)-2,3,4-trimethyl-2,5-diphenyloxazolidine **10** (1.50 g, 5.6 mmol). Colourless oil (1.18 g, 78%); $[\alpha]_D^{25}$ +92.5 (*c* 0.80, $CHCl_3$); ν_{max} (film)/cm^{-1} 3346, 3060, 3027, 2971, 2359, 1602, 1493, 1453, 1372, 1214, 1044, 920, 761, 700; δ_H (400 MHz; $CDCl_3$) 0.64 (3H, d, *J* 6.7 Hz), 1.46 (3H, d, *J* 6.6 Hz), 2.33 (3H, s), 2.68–2.72 (1H, m), 3.71 (1H, q, *J* 6.7 Hz), 4.17 (1H, d, *J* 9.4 Hz), 7.09–7.35 (10H, m); δ_C (100 MHz; $CDCl_3$) 7.9, 21.3, 31.4, 60.7, 62.5, 74.7, 127.3, 127.47, 127.52, 128.1, 128.6, 142.5, 148.0; *m*/*z* (ESI) 270.1848; $C_{18}H_{24}NO$ (MH^+) requires: 270.1858.

4.1.2.7. *N*-Methyl-*N*-((2*R*)-2-(1,4-dihydroxybutyl))-(1*R*,2*S*)-1-phenyl-2-aminopropanol (22)+enantiomer. Prepared according to the representative procedure from (−)-(2*R*,4*S*,5*R*)-2-(methoxycarbonylmethyl)-2-(methoxycarbonyl)-3,4-dimethyl-5-phenyloxazolidine **13** (2.00 g, 8.2 mmol) and DIBAL in hexanes (6 equiv). Colourless oil (1.56 g, 75%); $[\alpha]_D$ −4.0 (*c* 0.89, $CHCl_3$); ν_{max} (film)/cm^{-1} 3354, 3025, 2927, 1654, 1493, 1450, 1405, 1240, 1038, 758, 702; δ_H (400 MHz; $CDCl_3$) (mixture of diastereoisomers) 1.03 (3H, d, *J* 6.9 Hz, minor), 1.11 (3H, d, *J* 6.9 Hz, major), 1.40–1.50 (1H, m, major and 1H, m, minor), 1.60–1.70 (1H, m, minor), 1.70–1.90 (1H, m, major), 2.23 (3H, s, major), 2.30 (3H, s, minor), 2.81–3.15 (2H, m, major and 2H, m, minor), 3.30–355 (2H, m, major and 2H, m, minor), 3.60–3.75 (2H, m, major and 2H, m, minor), 4.84 (1H, d, *J* 5.0 Hz, major), 4.92 (1H, d, *J* 3.6 Hz, minor), 7.09–7.35 (5H, m, major and 5H, m, minor); δ_C (100 MHz; $CDCl_3$) (major diastereoisomer) 12.0, 30.2, 30.6, 60.9, 61.0, 62.0, 64.6, 74.7, 126.1, 127.4, 128.3, 1427; *m*/*z* (ESI) 254.1751; $C_{14}H_{24}NO_3$ (MH^+) requires: 254.1756.

4.1.2.8. (+)-(2*R*,4*S*,5*S*)-2-(1-(2-Hydroxyethyl))-2-(2-hydroxymethyl)-3,4-dimethyl-5-phenyloxazolidine (23). Prepared according to the representative procedure from (+)-(2*R*,4*S*,5*S*)-2-(methoxycarbonylmethyl)-2-(methoxycarbonyl)-3,4-dimethyl-5-phenyloxazolidine **14** (1.0 g, 3.26 mmol) and DIBAL in hexanes (4 equiv). Colourless oil (0.82 g, 63%); $[\alpha]_D^{25}$ +46.1 (*c* 1.08, $CHCl_3$); ν_{max} (film)/cm^{-1} 3388, 3060, 2963, 2870, 2348, 1604, 1494, 1454, 1377, 1258, 1058, 1022, 759, 701; δ_H (400 MHz; $CDCl_3$) 1.11 (3H, d, *J* 6.0 Hz), 1.78 (1H, ddd, *J* 1.6, 3.6, 15.2 Hz), 1.96–2.06 (1H, m), 2.49 (3H, s), 2.99–3.05 (1H, m), 3.66 (1H, d, *J* 11.6 Hz), 3.73 (1H, dt, *J* 3.6, 11.4 Hz), 3.80 (1H, d, *J* 11.4 Hz), 4.10–4.16 (1H, m), 4.67 (1H, d, *J* 8.8 Hz)

7.26–7.40 (5H, m); δ_C (100 MHz; $CDCl_3$) 14.8, 31.7, 33.1, 58.9, 64.7, 65.3, 86.6, 98.1, 127.0, 128.6, 128.7, 138.5; *m/z* (ESI) 252.1597; $C_{14}H_{22}NO_3$ (MH^+) requires: 252.1600.

4.1.2.9. (±)-*N*-Methyl-*N*-((2*R*)-2-(1,4-dihydroxybutyl))-(1*S*,2*S*)-1-phenyl-2-aminopropanol (24). Prepared according to the representative procedure from (+)-(2*R*,4*S*,5*S*)-2-(methoxycarbonylmethyl)-2-(methoxycarbonyl)-3,4-dimethyl-5-phenyloxazolidine **14** (0.50 g, 1.63 mmol). Colourless oil (0.33 g, 80%); $[\alpha]_D^{25}$ +39.5 (*c* 1.10, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3355, 3020, 2931, 1654, 1491, 1239; δ_H (400 MHz; $CDCl_3$) 0.86 (3H, d, *J* 6.7 Hz), 1.80–1.95 (1H, m), 2.33 (3H, s), 2.35–2.45 (1H, m), 2.55–3.10 (2H, m), 3.64–3.80 (4H, m), 4.25 (1H, d, 9.4 Hz), 7.26–7.40 (5H, m); δ_C (100 MHz; $CDCl_3$) 11.7, 30.5, 32.2, 57.1, 63.2, 63.8, 64.3, 77.0, 127.1, 128.5, 128.7, 138.0; *m/z* (ESI) 254.1754; $C_{14}H_{24}NO_3$ (MH^+) requires: 254.1756.

Acknowledgements

This investigation has enjoyed the support of the EPSRC and GlaxoSmithKline. We acknowledge the support of the Royal Society (P.C.B.P.: Industry Fellowship). We are indebted to the EPSRC Mass Spectrometry Service Centre, University of Wales, Swansea.

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