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Probing the parallel resolution of Mosher's acid using a combination of *quasi*-enantiomeric oxazolidin-2-ones

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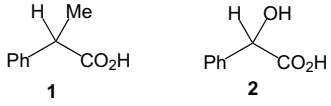
ABSTRACT

Mosher's acid (2-methoxy-2-phenyl-2-trifluoromethylacetic acid) was resolved by parallel resolution of its corresponding pentafluorophenyl active ester using a *quasi*-enantiomeric combination of oxazolidin-2-ones.

1. Introduction

The synthesis of enantiomerically pure carboxylic acids[1] based on the carbon-skeleton of phenylacetic acid, such as 2-phenylpropionic acid **1**[2] and Mandelic acid **2**,[3] are well documented (Scheme 1). Many of these derivatives have found widespread use as important biological[4] and synthetic intermediates.[5]

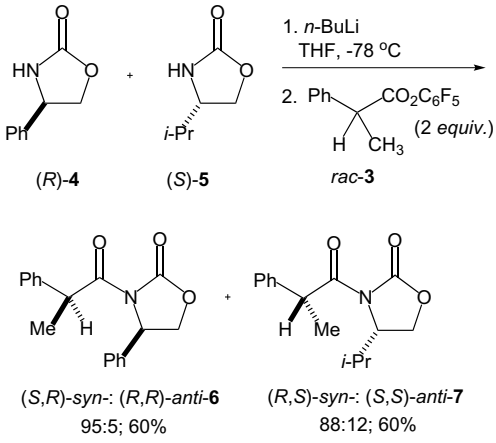


Scheme 1. 2-Phenylpropionic acid **1** and Mandelic acid **2**.

2. Results and discussion

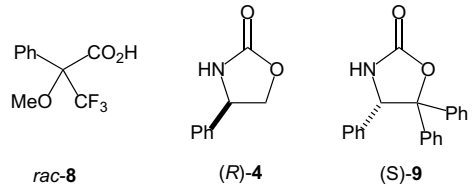
Over the last few years, we have been interested in the parallel kinetic resolution[6] of profen active esters,[7,8] such as pentafluorophenyl 2-phenylpropionate acid *rac*-**3**, using a combination of *quasi*-enantiomeric Evans' oxazolidin-2-ones (*R*)-**4** and (*S*)-**5** to give the corresponding adducts (*S*,*R*)-*syn*-**6** and (*R*,*S*)-*syn*-**7** in high yield and with excellent levels of diastereoselectivity (Scheme 2). We have already demonstrated that efficient molecular recognition and enantiomeric separation of active ester *rac*-**3** [to give the separable and complementary adducts (*S*,*R*)-*syn*-**6** and (*R*,*S*)-*syn*-**7**] can be readily achieved using a *quasi*-enantiomeric combination of oxazolidin-2-ones, (*R*)-**4** and (*S*)-**5**, respectively (Scheme 2).[7,9]

Herein we report an extension to our methodology for the resolution of Mosher's acid[10] (2-methoxy-2-phenyl-2-trifluoromethylacetic acid) *rac*-**8** using a *quasi*-enantiomeric combination of



Scheme 2. Parallel kinetic resolution of active ester *rac*-**3** using a *quasi*-enantiomeric combination of oxazolidin-2-ones (*R*)-**4** and (*S*)-**5**.

Evans'[11] and Seebach's oxazolidin-2-ones (*R*)-**4** and (*S*)-**9** (Scheme 3). We were interested in this particular[12] combination of oxazolidin-2-ones due to their ease of separation. The active ester *rac*-**10**



Scheme 3. Mosher's acid *rac*-**8**, and *quasi*-enantiomeric oxazolidin-2-ones (*R*)-**4** and (*S*)-**9**.

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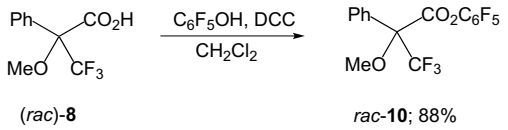


(*rac*)-**8** *rac*-**10**; 88%

Scheme 4. Synthesis of pentafluorophenyl 2-methoxy-2-phenyl-2-trifluoromethyl acetate *rac*-**10**.

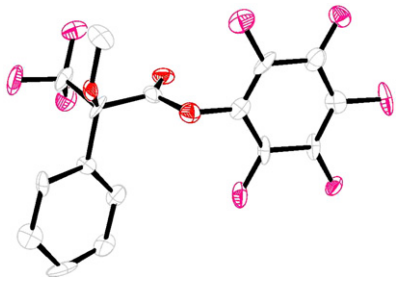
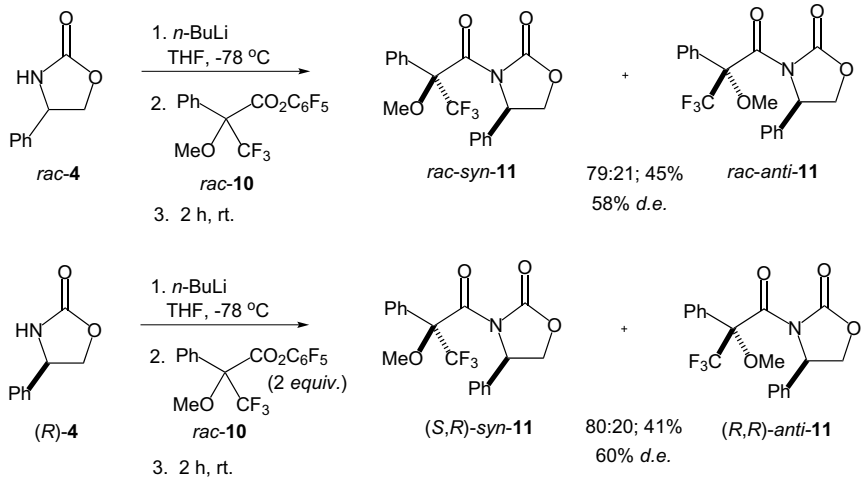


Figure 1. Molecular structure of pentafluorophenyl 2-methoxy-2-phenyl-2-trifluoromethyl acetate (*R*)-**10**, showing the atom labelling scheme. Displacement ellipsoids are drawn at 50% probability level and the H atoms have been omitted.[14]

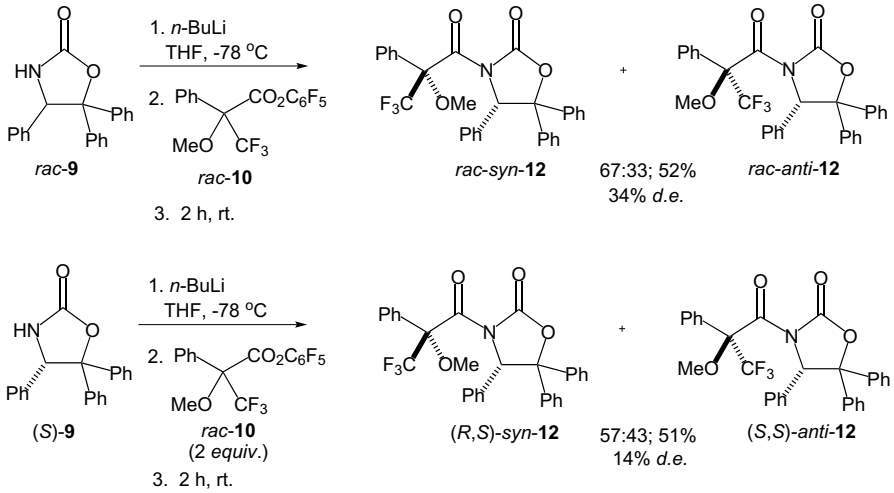
required for our study was synthesised in 88% yield by the addition of DCC to a stirred solution of pentafluorophenol and Mosher's acid *rac*-**8** in dichloromethane (Scheme 4 and Fig. 1).[13]

In order to get a measure of the potential enantiomeric recognition within our proposed parallel kinetic resolution, we first chose to probe the mutual recognition between the racemic active ester *rac*-**10** and racemic Evans' oxazolidin-2-one *rac*-**4** (Scheme 5). The addition of *n*-butyl lithium to a stirred solution of oxazolidin-2-one *rac*-**4** in THF at −78 °C, followed by the addition of active ester *rac*-**10**, and stirring the resulting solution at room temperature for 2 h, gave a separable mixture of diastereoisomeric adducts *rac-syn*- and *rac-anti*-**11** in 45% yield with good levels of diastereoisomeric control [ratio 79:21 (58% de)] (Scheme 5).[15] The relative levels of enantiomeric recognition and the overall levels of stereocontrol were found to be similar to those obtained from 2-methoxy-2-phenylacetic acid.[16,17]

We next investigated the complementary kinetic resolution of active ester *rac*-**10** using enantiomerically pure oxazolidin-2-one (*R*)-**4** (Scheme 5). This kinetic chemical resolution proved to be equally diastereoselective favouring the formation of oxazolidin-2-one (*S,R*)-*syn*-**11** [ratio (*S,R*)-*syn*-:(*R,R*)-*anti*-**11**: 80:20 (60% de)] in 41% yield (Scheme 5). With this information in hand, we next probed the complementary mutual and kinetic resolution of active



Scheme 5. Mutual and kinetic resolution of active ester *rac*-**10** using oxazolidin-2-ones *rac*- and (*R*)-**4**.

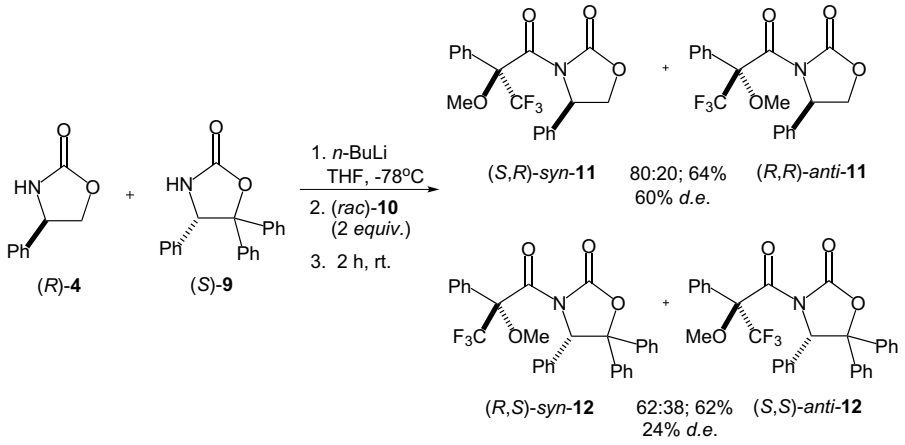


Scheme 6. Mutual and kinetic resolution of active ester *rac*-**10** using oxazolidin-2-ones *rac*- and (*S*)-**9**.

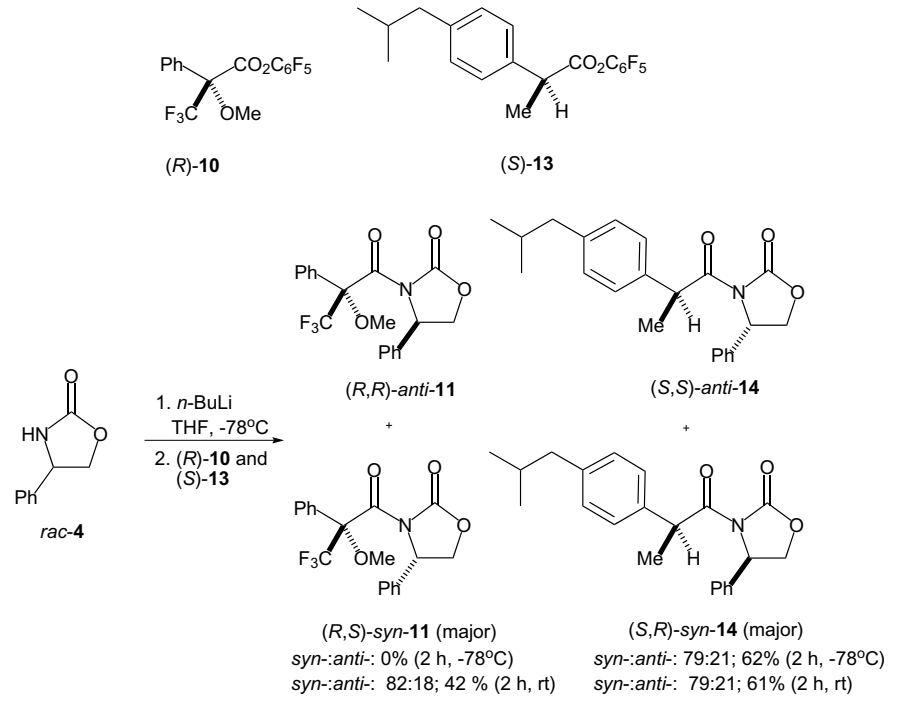
ester *rac*-**10**, using a more sterically-demanding oxazolidin-2-one, namely 4,5,5-triphenyl-oxazolidin-2-ones *rac*- and (*S*)-**9** (Scheme 6). These resolution processes proved to be slightly less stereoselective, favouring the formation of the oxazolidin-2-one adducts *rac*-*syn*- and (*R*,*S*)-*syn*-**12** with moderate levels of diastereoselectivities (14–34% diastereoisomeric excess) (Scheme 6).[15]

We first probed the parallel kinetic resolution of active ester *rac*-**10** using a *quasi*-enantiomeric combination of Evans' oxazolidin-2-one (*R*)-**4** and Seebach's oxazolidin-2-one (*S*)-**9** as we believed this would be a mimic for the mutual kinetic resolution of oxazolidin-2-one *rac*-**4** as outlined in Scheme 5. Deprotonation of a equimolar combination of oxazolidin-2-ones (*R*)-**4** and (*S*)-**9** using *n*-BuLi, followed by the addition of active ester *rac*-**10**, gave a pair of separable diastereoisomeric oxazolidin-2-ones (*S*,*R*)-*syn*- and (*R*,*R*)-*anti*-**11** (ratio 80:20; 64% yield) [derived from (*R*)-**4**] and (*R*,*S*)-*syn*- and (*S*,*S*)-*anti*-**12** (ratio 62:38; 62% yield) [derived from (*S*)-**9**], respectively (Scheme 7). The levels of diastereocontrol were found to be similar to their complementary mutual kinetic resolutions of active ester *rac*-**10** involving oxazolidin-2-ones *rac*-**4** and *rac*-**9**, respectively, and the resulting oxazolidin-2-one adducts were separated efficiently by column chromatography ($\Delta R_F = 0.32$) (Schemes 5 and 6).

In an attempt to improve the levels of diastereocontrol, we next probed the parallel kinetic resolution of Evans' oxazolidin-2-one *rac*-**4** using a *quasi*-enantiomeric mixture of active esters (*R*)-**10** [derived from Mosher's acid (*R*)-**8**] and (*S*)-**13** [derived from (*S*)-Ibuprofen][18] (Scheme 8). The addition of an equimolar amount of active esters (*R*)-**10** and (*S*)-**13** to a stirred solution of the lithiated oxazolidin-2-one [derived from the addition of *n*-butyl lithium to oxazolidin-2-one *rac*-**4**], gave the corresponding diastereoisomeric adducts (*R*,*S*)-*syn*-**11** and (*S*,*R*)-*syn*-**14** with high to moderate levels of diastereoselectivity (58–64% de) (Scheme 8). The level of diaste-



Scheme 7. Parallel kinetic resolution of active ester *rac*-**10** using a *quasi*-enantiomeric combination of oxazolidin-2-ones (*R*)-**4** and (*S*)-**9**.

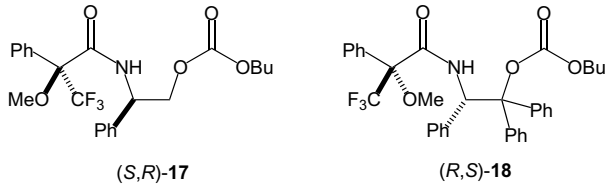


Scheme 8. Sequential kinetic resolution of oxazolidin-2-one *rac*-**4** using a *quasi*-enantiomeric combination of active esters (*R*)-**10** and (*S*)-**13**.

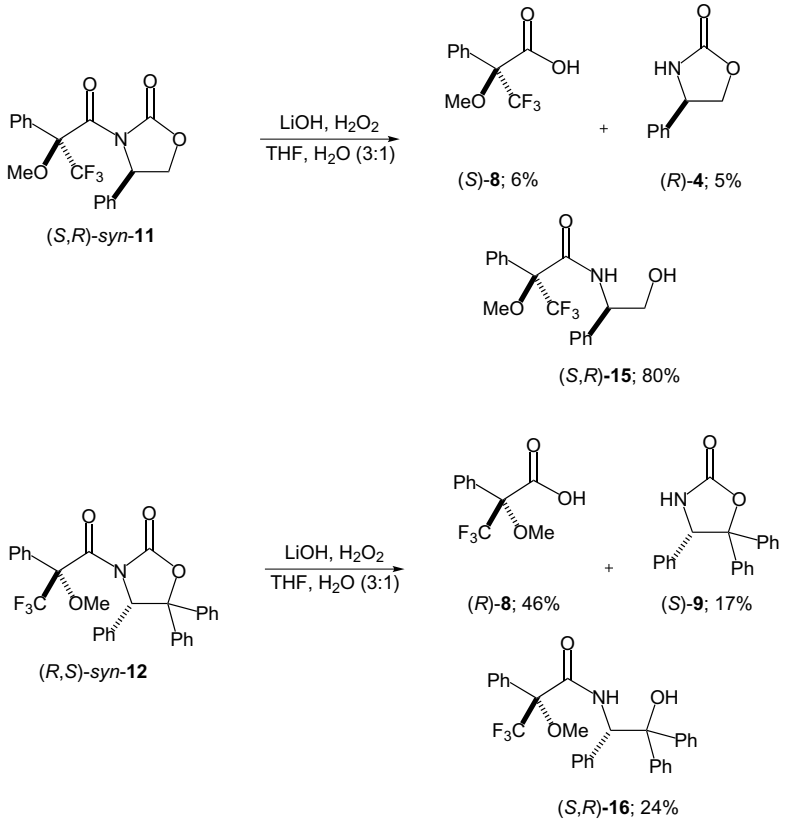
reocontrol for (*S*,*R*)-*syn*-**14** was comparable to that of its kinetic resolution,[19] whereas for (*R*,*R*)-*anti*-**11**, the diastereoselectivity was significantly higher (Scheme 8). However, by quenching this resolution after 2 h at −78 °C, only the less sterically-demanding active ester (*S*)-**13** [derived from (*S*)-Ibuprofen][18] appeared to have reacted with the lithiated oxazolidin-2-one to give the corresponding adduct (*S*,*R*)-*syn*-**14** in a similar yield (62%) with comparable diastereoselectivity (58% de) to that previously obtained (Scheme 8).[20] This rate difference and the resulting increase in concentration of active ester (*R*)-**10** appears to be sufficient[21] enough to increase the levels of diastereocontrol for the (*R*,*S*)-*syn*-**11** through a sequential (parallel) kinetic resolution (SPKR) (Scheme 8). These resulting adducts **11** and **14** were efficiently separated by column chromatography.

With these oxazolidin-2-one adducts (*S*,*R*)-*syn*-**11** and (*R*,*S*)-*syn*-**12** in hand, we next investigated their hydrolysis using a combination of lithium hydroxide monohydrate and hydrogen peroxide in a mixture of THF/H_2O (3:1). Treatment of oxazolidin-2-ones (*S*,*R*)-*syn*-**11** and (*R*,*S*)-*syn*-**12** with LiOH/H_2O_2 in THF/H_2O (3:1) at rt for 12 h, gave the corresponding Mosher's acids (*S*)- and (*R*)-**8** in 6% and 46% yields, respectively (Scheme 9). The resulting oxazolidin-2-ones (*R*)-**4** and (*S*)-**9** were recovered in related 5% and 17% yields,[22] respectively (Scheme 9). The overall yield for these seemingly simple hydrolyses were low due to competitive *endo*-cleavage of the oxazolidin-2-one adducts (*S*,*R*)-*syn*-**11** and (*R*,*S*)-*syn*-**12** to give the corresponding amides (*S*,*R*)-**15** and (*R*,*S*)-**16** in 80% and 24% yields (Scheme 9). This type of *endo*-cleavage[23] is unsurprising for sterically-demanding oxazolidin-2-one adducts, such as (*S*,*R*)-*syn*-**11**, where *exo*-cleavage is evidently disfavoured due to steric hindrance [(*S*,*R*)-**15**:(*R*)-**4** ratio 92:8—determined by 400 MHz ^{1}H NMR spectroscopy]. For *C*(5)-disubstituted oxazolidin-2-ones, such as Seebach's oxazolidin-2-one **9**, which were designed to disfavour this type of *endo*-cleavage pathway,[12,23,24] do favour the required *exo*-cleavage pathway [(*R*,*S*)-**16**:(*S*)-**9** ratio 33:67—determined by 400 MHz ^{1}H NMR spectroscopy] to give the Mosher's acid (*R*)-**8** in 46% yield (Scheme 9).

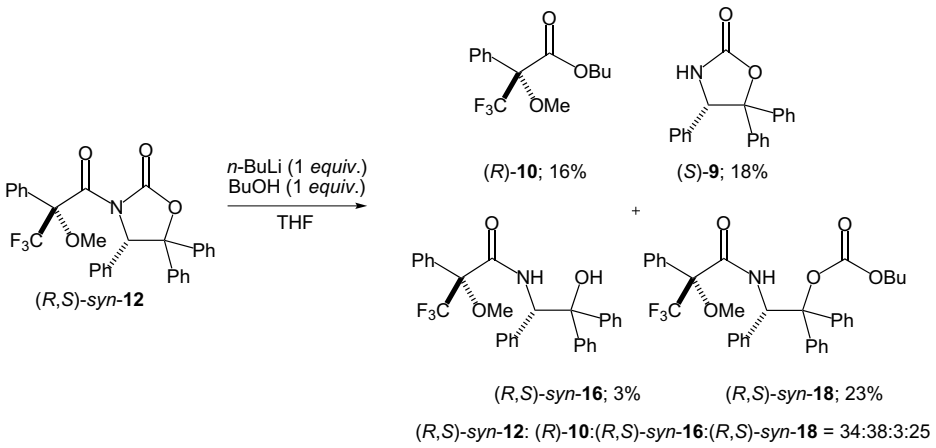
Further evidence for this unusual *endo*-cleavage pathway can be seen from the formation of two by-products, amides (*S*,*R*)-*syn*-**17** (formed in 9–15%) and (*S*,*R*)-*syn*-**18** (formed in 5–13%), derived from the addition of lithium butoxide [a contaminant present in varying amounts in *n*-BuLi (in hexane) due to reaction with molecular O_2] to the corresponding oxazolidin-2-one adducts (*S*,*R*)-*syn*-**11** and (*S*,*R*)-*syn*-**12** (Scheme 10). The amount of amides **17** and **18** formed were found to be dependent on the quality of the *n*-BuLi/hexane solution, THF[25] used and the reaction time. These amide adducts [e.g., (*R*,*S*)-*syn*-**18**] can be synthesised in moderate yield (23%) by addition of LiOBu (formed by addition of *n*-BuLi to BuOH in THF) to a stirred solution oxazolidin-2-one (*R*,*S*)-*syn*-**12** in THF at −78 °C (Scheme 11). However, the addition of an excess amount of lithium butoxide (2 equiv) to (*S*,*R*)-*syn*-**11** and (*R*,*S*)-*syn*-



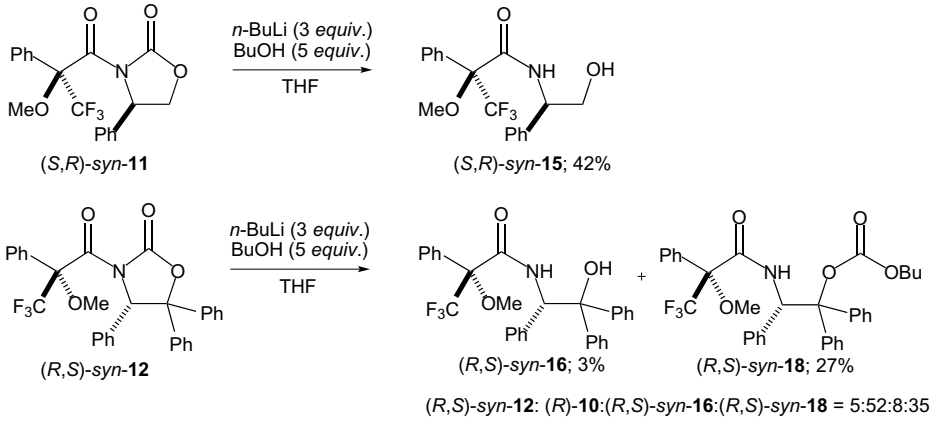
Scheme 10. Formation of amides (*S*,*R*)-*syn*-**17** and (*R*,*S*)-*syn*-**18** by in situ *endo*-cleavage of (*S*,*R*)-*syn*-**11** and (*R*,*S*)-*syn*-**12**.



Scheme 9. *Exo*- and *endo*-cleavage of oxazolidin-2-one adducts (*S*,*R*)-*syn*-**11** and (*R*,*S*)-*syn*-**12**.



Scheme 11. Formation of amides (*R*,*S*)-*syn*-**16** and (*R*,*S*)-*syn*-**18** by in situ *endo*-cleavage of (*R*,*S*)-*syn*-**12**.



Scheme 12. Formation of amides (*S*,*R*)-*syn*-**15** and (*R*,*S*)-*syn*-**18** by in situ *endo*-cleavage of (*S*,*R*)-*syn*-**11** and (*R*,*S*)-*syn*-**12**.

12 gave the corresponding amides (*S*,*R*)-*syn*-**15** and (*R*,*S*)-*syn*-**16** in 42% and 3%, respectively, through butoxycarbonyl cleavage of the intermediate carbonates (*S*,*R*)-*syn*-**17** and (*R*,*S*)-*syn*-**18**, respectively (Scheme 12). Interestingly, for (*R*,*S*)-*syn*-**12** using an excess of *n*-BuLi (3 equiv), the relative amount of *exo*- and *endo*-cleavage remained unchanged [ratio—53:47 (1 equiv of *n*-BuOLi) and 55:45 (3 equiv of *n*-BuOLi), respectively], whereas, the relative proportion of (*R*,*S*)-*syn*-**16** increased [from 11:89 to 23:77 for (*R*,*S*)-*syn*-**16**:(*R*,*S*)-*syn*-**18**] through competitive butoxycarbonyl cleavage of (*R*,*S*)-*syn*-**18** to give (*R*,*S*)-*syn*-**16** and dibutylcarbonate.[26] Whereas, for the less sterically-demanding oxazolidin-2-one (*S*,*R*)-*syn*-**11**, exclusive *endo*-cleavage was preferred to give the amide (*S*,*R*)-*syn*-**15** in 42% yield via a double *n*-BuOLi addition process (Scheme 12).

3. Conclusion

In conclusion, we have demonstrated the parallel resolution of Mosher's acid *rac*-**8** using a combination of *quasi*-enantiomeric oxazolidin-2-ones as mutual resolving components. The overall levels of diastereoselectivity were shown to be good (up to 60% de). This level of mutual recognition could be increased to 64% de via the use of differentially selective surrogate active esters, such as (*S*)-**3** or (*S*)-**13**, using a sequential parallel kinetic resolution approach. Hydrolysis of the resulting adducts leads to competitive *endo*- and *exo*-cleavage pathways.

4. Experimental

4.1. General

All solvents were distilled before use. All reactions were carried out under nitrogen using oven-dried glassware. Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). Thin layer chromatography (TLC) was carried out on commercially available pre-coated plates (Merck Kieselgel 60F_{254} silica). Proton and carbon NMR spectra were recorded on a Bruker 400 MHz Fourier transform spectrometer using an internal deuterium lock. Chemical shifts are quoted in parts per million downfield from tetramethylsilane. Carbon NMR spectra were recorded with broad proton decoupling. Infrared spectra were recorded on a Shimadzu 8300 FTIR spectrometer. Optical rotation was measured using an automatic AA-10 Optical Activity Ltd polarimeter.

4.1.1. Pentafluorophenyl 1-trifluoromethyl-1-methoxy-phenylacetate (*R*)-10

N,*N*′-Dicyclohexylcarbodiimide (DCC) (1.75 g, 8.49 mmol) was slowly added to a stirred solution of 1-trifluoromethyl-1-methoxy-phenylacetic acid (*R*)-**8** (1.80 g, 7.71 mmol) in dichloromethane (10 ml) at room temperature. The resulting solution was stirred for 15 min. A solution of pentafluorophenol (1.41 g, 7.71 mmol) in dichloromethane (3 ml) was slowly added and the resulting solution was stirred for a further 2 h. The resulting white

precipitate (dicyclohexylurea) was removed through filtration (using a sintered funnel). The reaction was quenched with water (20 ml) and extracted with dichloromethane (3 × 10 ml). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (9:1) to give the pentafluorophenyl 1-trifluoromethyl-1-methoxy-phenylacetate (*R*)-**10** (2.86 g, 92%) as needle-like crystals; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (9:1)] 0.78; mp 43–44 °C (lit.[27] 45 °C); $\nu_{max}(CH_2Cl_2)$ cm^{-1} 3056, 2999, 2938 and 2854 (C–H aromatic), 1790 (C=O), and 1266 and 1176 (C–F); $[\alpha]_D^{22} = +42.4$ (*c* 1.02, $CHCl_3$) [lit.[27] +43.5] {for (*S*)-**10** $[\alpha]_D^{22} = -47.1$ (*c* 1.22, $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 7.62–7.60 (2H, m, 2 × CH; Ph), 7.49–7.45 (3H, m, 3 × CH; Ph) and 3.69 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 163.2 (C=O), 140.9 (142.25 and 139.73, 2C, ddt, $^1J_{C,F}$ = 253.1 Hz, $^2J_{C,F}$ = 12.0 Hz and $^3J_{C,F}$ = 4.6 Hz, C(2)–F), 140.1 (141.37 and 138.83, 1C, dtt, $^1J_{C,F}$ = 254.0 Hz, $^2J_{C,F}$ = 13.8 Hz and $^3J_{C,F}$ = 3.8 Hz, C(4)–F), 138.0 (139.24 and 136.89, 2C, dtdd, $^1J_{C,F}$ = 249.0 Hz, $^2J_{C,F}$ = 12.9 Hz, $^3J_{C,F}$ = 5.3 and $^4J_{C,F}$ = 3.0 Hz, C(3)–F), 130.9 (*i*-C; Ph), 130.3,[2] 128.7,[2] 127.2[1] (5 × CH; Ph), 124.2 (1C, tdt, $^2J_{C,F}$ = 14.2 Hz, $^4J_{C,F}$ = 4.6 Hz and $^3J_{C,F}$ = 2.3 Hz, *i*-CO; OC_6F_5), 122.9 (1C, q, $^1J_{CF}$ 288.2, CF_3), 85.4 (1C, q, $^2J_{CF}$ 28.4, PhCCF_3) and 56.5 (CH_3O); δ_F (378 MHz, $CDCl_3$) −71.8 (1C, s, CF_3), −151.4 (2C, d, $^3J_{CF}$ 18.5, *o*-CF; C_6F_5), −155.8 (1C, d, $^3J_{CF}$ 18.5, *p*-CF; C_6F_5) and −161.1 (2C, d, $^3J_{CF}$ 18.5, *m*-CF; C_6F_5); *m*/*z* 189.1 (100%, $PhC^+(CF_3)OMe$).

4.1.2. Pentafluorophenyl 1-trifluoromethyl-1-methoxy-phenylacetate *rac*-10

In the same way as above, *N*,*N*′-dicyclohexylcarbodiimide (DCC) (0.71 g, 3.44 mmol), 1-trifluoromethyl-1-methoxy-phenylacetic acid (*R*)-**8** (0.74 g, 3.16 mmol) and pentafluorophenol (0.58 g, 3.16 mmol) in dichloromethane (10 ml) gave after purification by column chromatography on silica gel eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (9:1) pentafluorophenyl 1-trifluoromethyl-1-methoxy-phenylacetate *rac*-**10** (1.11 g, 88%) as needle-like crystals; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (9:1)] 0.87; mp 80–82 °C; ν_{max} (CH_2Cl_2) cm^{-1} 3057 and 2854 (C–H aromatic), 1790 (C=O), and 1266 and 1176 (C–F); δ_H (400 MHz, $CDCl_3$) 7.65–7.59 (2H, m, 2 × CH; Ph), 7.50–7.43 (3H, m, 3 × CH; Ph) and 3.70 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 163.3 (C=O), 140.9 (142.20 and 139.67, 2C, ddt, $^1J_{C,F}$ = 253.1 Hz, $^2J_{C,F}$ = 12.0 Hz and $^3J_{C,F}$ = 4.6 Hz, C(2)–F), 140.0 (141.32 and 138.78, 1C, dtt, $^1J_{C,F}$ = 254.0 Hz, $^2J_{C,F}$ = 13.8 Hz and $^3J_{C,F}$ = 3.8 Hz, C(4)–F), 137.9 (139.19 and 136.70, 2C, dtdd, $^1J_{C,F}$ = 249.0 Hz, $^2J_{C,F}$ = 12.9 Hz, $^3J_{C,F}$ = 5.3 and $^4J_{C,F}$ = 3.0 Hz, C(3)–F), 130.9 (*i*-C; Ph), 130.2,[2] 128.6,[2] 127.1[1] (5 × CH; Ph), 124.1 (1C, tdt, $^2J_{C,F}$ = 14.2 Hz, $^4J_{C,F}$ = 4.6 Hz and $^3J_{C,F}$ = 2.3 Hz, *i*-CO; OC_6F_5), 122.8 (1C, q, $^1J_{CF}$ 288.2, CF_3), 85.3 (1C, q, $^2J_{CF}$ 28.4, PhCCF_3) and 56.4 (CH_3O); δ_F (378 MHz, $CDCl_3$) −71.8 (1C, s, CF_3), −151.4 (2C, d, $^3J_{CF}$ 18.5, *o*-CF; C_6F_5), −155.9 (1C, d, $^3J_{CF}$ 18.5, *p*-CF; C_6F_5) and −161.3 (2C, d, $^3J_{CF}$ 18.5, *m*-CF; C_6F_5); *m*/*z* 189.1 (100%, $PhC^+(CF_3)OMe$).

4.1.3. (*SR*,*RS*)-4-Phenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one *rac-syn*-11 and (*RS*,*RS*)-4-phenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one *rac-anti*-11—mutual kinetic resolution of active ester *rac*-10 using oxazolidin-2-one *rac*-4

n-BuLi (0.60 ml, 2.5 M in hexane, 1.50 mmol) was added to a stirred solution of oxazolidin-2-one *rac*-**4** (0.205 g, 1.26 mmol) in THF (50 ml) at −78 °C. After stirring for 1 h, a solution of active ester *rac*-**10** (0.61 g, 1.52 mmol) in THF (10 ml) was slowly added. The resulting solution was stirred for 2 h at −78 °C and then allowed to warm up to room temperature. The resulting solution was stirred for a further 2 h. The reaction was quenched with water (10 ml) and extracted with diethyl ether (2 × 20 ml). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (1:1) to give a separable diastereoisomeric mixture (*syn*-:*anti*- 79:21) of oxazolidin-2-one *rac-syn*-**11** (0.17 g, 36 %) as plate-like crystals; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.35; mp 158–160 °C; $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1796 (C=O), 1702 (C=O) and 1262 (C–F); δ_H (400 MHz, $CDCl_3$) 7.46–7.41 (2H, m, 2 × CH; Ph), 7.37–7.27 (8H, m, 8 × CH; Ph), 5.56 (1H, dd, *J* 6.0 and 2.5, PhCHN), 4.60 (1H, t, *J* 6.0, C$H_A$$H_B$O), 4.26 (1H, dd, *J* 6.0 and 2.5, CH_AH_BO) and 3.52 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 166.6 (NC=O), 150.1 (OC=O), 138.6 (*i*-C; Ph), 132.2 (*i*-C; Ph), 129.7,[1] 129.6,[3] 129.5,[1] 128.4,[2] 127.1[1] and 127.0[2] (10 × CH; 2 × Ph), 123.6 (1C, q, $^1J_{CF}$ 291.2, CF_3), 86.2 (1C, q, $^2J_{CF}$ 25.9, PhCCF_3), 70.4 (CH_2O), 59.1 (PhCHN) and 56.5 (1C, d, $^4J_{CF}$ 1.9, CH_3O); δ_F (378 MHz, $CDCl_3$) −71.0 (1C, s, CF_3) (Found MNH_4^+ 397.1372. $C_{19}H_{20}F_3N_2O_4$ requires MNH_4^+, 379.1370); and the oxazolidin-2-one *rac-anti*-**11** (43 mg, 9 %) as a pale yellow oil; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.13; ν_{max} (CH_2Cl_2)/cm^{-1} 1803 (C=O), 1702 (C=O) and 1256 (C–F); δ_H (400 MHz, $CDCl_3$) 7.34–7.13 (10H, m, 2 × CH; 2 × Ph), 5.25 (1H, dd, *J* 8.0 and 2.0, PhCHN), 4.43 (1H, dd, *J* 8.8 and 8.0, C$H_A$$H_B$O), 4.08 (1H, dd, *J* 8.8 and 2.0, CH_AH_BO) and 3.42 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 165.2 (NC=O), 149.9 (OC=O), 138.5 (*i*-C; Ph), 132.0 (*i*-C; Ph), 129.4,[1] 129.1,[3] 129.0,[1] 128.0,[2] 126.6[1] and 126.0[2] (10 × CH; 2 × Ph), 123.2 (1C, q, $^1J_{CF}$ 290.4, CF_3), 85.7 (1C, q, $^2J_{CF}$ 26.1, PhCCF_3), 70.0 (CH_2O), 58.8 (PhCHN) and 56.1 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −70.7 (1C, s, CF_3) (Found MNH_4^+ 397.1370. $C_{19}H_{20}F_3N_2O_4$ requires MNH_4^+, 397.1370).

4.1.4. Kinetic resolution of active ester *rac*-10 using oxazolidin-2-one (*R*)-4; synthesis of (*S*,*R*)-4-phenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one *syn*-11

In the same way as above, *n*-butyl lithium (0.35 ml, 2.5 M in hexane, 0.88 mmol), oxazolidin-2-one (*R*)-**4** (0.12 g, 0.74 mmol) and active ester *rac*-**10** (0.59 g, 1.47 mmol) gave a crude mixture of oxazolidin-2-ones (*S*,*R*)-*syn*- and (*R*,*R*)-*anti*-**11** (ratio 79:21). This residue was purified by column chromatography on silica gel eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (9:1) to give the oxazolidin-2-one (*S*,*R*)-*syn*-**11** (38 mg, 33%) as a white crystalline solid; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.35; mp 173–175 °C; $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1796 (C=O), 1702 (C=O) and 1262 (C–F); $[\alpha]_D^{22} = -17.4$ (*c* 1.4, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.45–7.42 (2H, m, 2 × CH; Ph), 7.35–7.26 (8H, m, 8 × CH; 2 × Ph), 5.50 (1H, dd, *J* 6.0 and 2.5, PhCHN), 4.55 (1H, t, *J* 6.0, C$H_A$$H_B$O), 4.22 (1H, dd, *J* 6.0 and 2.5, CH_AH_BO) and 3.45 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 166.3 (NC=O), 149.7 (OC=O), 138.1 (*i*-CC; Ph), 131.8 (*i*-C; Ph), 129.3,[1] 129.2,[3] 129.0,[1] 127.6,[2] 126.6[1] and 126.5[2] (10 × CH; 2 × Ph), 123.3 (1C, q, $^1J_{CF}$ 291.3, CF_3), 85.6 (1C, q, $^2J_{CF}$ 26.2, PhCCF_3), 69.9 (CH_2O), 58.7 (PhCHN) and 56.0 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −71.0 (1C, s, CF_3) (Found MNH_4^+ 397.1372. $C_{19}H_{20}F_3N_2O_4$ requires MNH_4^+, 379.1370); and the oxazolidin-2-one (*R*,*R*)-*anti*-**11** (9 mg, 8%) as white crystalline solid; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.13; mp 86–88 °C; ν_{max} (CH_2Cl_2) cm^{-1} 1803 (C=O), 1702 (C=O) and 1256 (C–F); $[\alpha]_D^{22} = +136.4$ (*c* 1.07, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.34–7.13 (10H, m, 2 × CH; 2 × Ph), 5.25 (1H, dd, *J* 7.8 and 2.0, PhCHN), 4.43 (1H, dd, *J* 8.8 and 8.0, C$H_A$$H_B$O), 4.08 (1H, dd, *J* 8.8 and 2.0, CH_AH_BO), 3.42 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 165.2 (NC=O), 149.9 (OC=O), 138.5 (*i*-CC; Ph), 132.0 (*i*-CC; Ph), 129.4,[1] 129.1,[3] 129.0,[1] 128.0,[2] 126.6[1] and 126.0[2] (10 × CH; 2 × Ph), 123.2 (1C, q, $^1J_{CF}$ 290.4, CF_3), 85.7 (1C, q, $^2J_{CF}$ 26.1, PhCCF_3), 70.0 (CH_2O), 58.8 (PhCHN) and 56.1 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −70.7 (1C, s, CF_3) (Found MNH_4^+ 397.1370. $C_{19}H_{20}F_3N_2O_4$ requires MNH_4^+, 397.1370).

4.1.5. Mutual kinetic resolution of active ester *rac*-10 using oxazolidin-2-one *rac*-9; synthesis of (*SR*,*RS*)-4-phenyl-5,5-diphenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one *rac-syn*-12 and (*RS*,*RS*)-4-phenyl-5,5-diphenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one *rac-anti*-12

In the same way as above, *n*-butyl lithium (0.25 ml, 2.5 M in hexane, 0.63 mmol), oxazolidin-2-one *rac*-**9** (0.17 g, 0.54 mmol) and active ester *rac*-**10** (0.25 g, 0.62 mmol) gave a crude mixture of oxazolidin-2-ones *rac-syn*-and *rac-anti*-**12** (ratio 67:33). This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (1:1) to give an inseparable mixture (ratio 67:33) of oxazolidin-2-ones *rac-syn*- and *rac-anti*-**12** (149 mg, 52%) as a white solid; mp 182–185 °C.

Characterisation data for [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.77; $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1792 (C=O), 1715 (C=O) and 1267 (C–F); δ_H (400 MHz, $CDCl_3$) 7.53–7.47 (2H, m, 2 × CH; Ph), 7.40–7.30 (4H, m, 4 × CH, 2 × Ph), 7.10 (1H, t, *J* 7.3, CH; Ph), 7.05–6.85 (13H, m, 13 × CH; 4 × Ph), 6.23 (1H, s, PhCHN) and 3.35 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 165.6 (NC=O), 149.0 (OC=O), 141.7, 137.2, 135.1 and 131.4 (4 × *i*-C; Ph), 129.0,[2] 128.9,[1] 128.8,[1] 128.4,[1] 128.3,[2] 127.8,[2] 127.7,[2] 127.6,[2] 127.5,[2] 126.4,[1] 125.9[2] and 125.5[2] (20 × CH; 4 × Ph), 123.3 (1C, q, $^1J_{CF}$ 290.4, CF_3), 89.2 (*C*(Ph)$_2$O), 85.4 (1C, $^2J_{CF}$ 25.4, Ph*C*), 67.6 (PhCHN) and 56.0 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −71.7 (1C, s, CF_3) (Found MNa^+ 554.1548. $C_{31}H_{24}F_3NO_4Na$ requires MNa^+, 554.1550).

rac-anti-**12**; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.77; ν_{max} (CH_2Cl_2) cm^{-1} 1807 (C=O), 1702 (C=O) and 1256 (C–F); δ_H (400 MHz, $CDCl_3$) 7.52 (2H, d, *J* 7.4, 2 × CH; Ph), 7.35–7.18 (8H, m, 8 × CH, 3 × Ph), 7.09–7.05 (3H, m, 3 × CH, Ph), 6.95 (7H, m, 7 × CH; 3 × Ph), 6.00 (1H, s, PhCHN) and 2.92 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 165.3 (NC=O), 149.0 (OC=O), 141.2, 136.9, 134.8 and 132.1 (4 × *i*-C; Ph), 129.3,[1] 129.0,[2] 128.8,[1] 128.5,[1] 128.3,[2] 128.0,[2] 127.7,[2] 127.6,[1] 127.4,[2] 126.5,[2] 125.8[2] and 125.5[2] (20 × CH; 4 x Ph), 123.1 (1C, q, $^1J_{CF}$ 290.5, CF_3), 89.1 (*C*(Ph)$_2$O), 85.6 (1C, $^2J_{CF}$ 25.4, Ph*C*), 67.7 (PhCHN) and 55.3 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −70.3 (1C, s, CF_3) (Found MH^+ 532.1732. $C_{31}H_{25}F_3NO_4$ requires MH^+, 532.1732).

4.1.6. Kinetic resolution of active ester (*S*)-10 using oxazolidin-2-one (*S*)-9; synthesis of (*R*,*S*)-4-phenyl-5,5-diphenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one *syn*-12

In the same way as above, *n*-butyl lithium (0.10 ml, 2.5 M in hexane, 0.24 mmol), oxazolidin-2-one (*S*)-**9** (68 g, 0.22 mmol) and active ester *rac*-**10** (0.17 g, 0.43 mmol) gave a crude mixture of oxazolidin-2-ones (*R*,*S*)-*syn*-**12** and (*S*,*S*)-*anti*-**12** (ratio 57:43). This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (1:1) to give racemic butyl 2-phenyl-2-methoxy-2-trifluoromethyl acetate (23 mg, 18 %) as a colourless oil; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.87; $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1747 (C=O); δ_H (400 MHz, $CDCl_3$) 7.51–7.45 (2H, m, 2 × CH; Ph^S), 7.53–7.48 (2H, m, 2 × CH; Ph), 7.41–7.36 (3H, m, 3 × CH; Ph), 4.36–4.25 (2H, m, CH_2O), 3.53 (3H, q, $^4J_{CF}$ 1.1, OCH_3), 1.70–1.62 (2H, m, CH_2), 1.39–1.30 (2H, appears as a br sextet, *J* 7.3, CH_2) and 0.89 (3H, t, *J* 7.5, C*H*$_3$CH$_2$); δ_C (100 MHz, $CDCl_3$) 166.5 (C=O), 132.3 (*i*-C; Ph), 129.5,[1] 128.3[2] and 127.2[2] (5 × CH; Ph), 124.1 (1C, q, $^1J_{CF}$ 286.5, CF_3), 84.5 (1C, q, $^2J_{CF}$ 26.7, Ph*C*CF_3), 66.2 (CH_2O), 55.3 (OCH_3), 30.3 (CH_2), 18.9 (CH_2) and 13.4 (CH_3); δ_F (378 MHz, $CDCl_3$) −71.5 (1C, s, CF_3) (Found MNH_4^+ 308.1467. $C_{14}H_{21}F_3NO_3$ requires MNH_4^+, 308.1468); and an inseparable diastereoisomeric mixture (*syn*-:*anti*-: 57:43) of oxazolidin-2-ones, (*R*,*S*)-*syn*- and (*S*,*S*)-*anti*-**12** (59 mg, 51%) as a colourless oil.

Characterisation data for oxazolidin-2-one (*R*,*S*)-*syn*-**12**; $[\alpha]_D^{25} = -2.7$ (*c* 0.9, $CHCl_3$)}; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.77; ν_{max} (CH_2Cl_2) cm^{-1} 1792 (C=O), 1715 (C=O) and 1267 (C–F); δ_H (400 MHz, $CDCl_3$) 7.53–7.47 (2H, m, 2 × CH; Ph), 7.40–7.30 (4H, m, 4 × CH, 2 × Ph), 7.10 (1H, t, *J* 7.3, CH; Ph), 7.05–6.85 (13H, m, 13 × CH; 4 × Ph), 6.23 (1H, s, PhCHN) and 3.35 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 165.6 (NC=O), 149.0 (OC=O), 141.7, 137.2, 135.1 and 131.4 (4 × *i*-C; Ph), 129.0,[2] 128.9,[1] 128.8,[1] 128.4,[1] 128.3,[2] 127.8,[2] 127.7,[2] 127.6,[2] 127.5,[2] 126.4,[1] 125.9[2] and 125.5[2] (20 × CH; 4 × Ph), 123.3 (1C, q, $^1J_{CF}$ 290.4, CF_3), 89.2 (*C*(Ph)$_2$O), 85.4 (1C, $^2J_{CF}$ 25.4, Ph*C*), 67.6 (PhCHN) and 56.0 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −71.7 (1C, s, CF_3) (Found MNa^+ 554.1548. $C_{31}H_{24}F_3NO_4Na$ requires MNa^+, 554.1550); and oxazolidin-2-one (*S*,*S*)-*anti*-**12**; $[\alpha]_D^{25} = -232.4$ (*c* 1.05, $CHCl_3$); R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.77; $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1807 (C=O), 1702 (C=O) and 1256 (C–F); δ_H (400 MHz, $CDCl_3$) 7.52 (2H, d, *J* 7.4, 2 × CH; Ph), 7.35–7.18 (8H, m, 8 × CH, 3 × Ph), 7.09–7.05 (3H, m, 4 × CH, Ph), 6.95 (7H, m, 7 × CH; 3 × Ph), 6.00 (1H, s, PhCHN) and 2.92 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 165.3 (NC=O), 149.0 (OC=O), 141.2, 136.9, 134.8 and 132.1 (4 × *i*-C; Ph), 129.3,[1] 129.0,[2] 128.8,[1] 128.5,[1] 128.3,[2] 128.0,[2] 127.7,[2] 127.6,[1] 127.4,[2] 126.5,[2] 125.8[2] and 125.5[2] (20 × CH; 4 × Ph), 123.1 (1C, q, $^1J_{CF}$ 290.5, CF_3), 89.1 (*C*(Ph)$_2$O), 85.6 (1C, $^2J_{CF}$ 25.4, Ph*C*), 67.7 (PhCHN) and 55.3 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −70.3 (1C, s, CF_3) (Found MH^+ 532.1732. $C_{31}H_{25}F_3NO_4$ requires MH^+, 532.1732).

4.1.7. Parallel kinetic resolution of racemic active ester *rac*-10 using a combination of *quasi*-enantiomeric combination of oxazolidin-2-ones (*R*)-4 and (*S*)-9

In the same way as above, *n*-butyl lithium (0.44 ml, 2.5 M in hexane, 1.10 mmol), oxazolidin-2-one (*R*)-**4** (75 mg, 0.46 mmol), oxazolidin-2-one (*S*)-**9** (0.148 g, 0.47 mmol) and active ester *rac*-**10** (0.44 g, 1.10 mmol) gave a crude mixture of oxazolidin-2-ones (*R*,*R*)-*anti*- and (*S*,*R*)-*syn*-**11** (ratio: 20:80; 64%) and (*S*,*S*)-*anti*- and (*R*,*S*)-*syn*-**12** (ratio: 38:62; 62%). This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (8:2) to give an inseparable mixture of oxazolidin-2-ones (*R*,*R*)-*anti*- and (*S*,*R*)-*syn*-**11** (0.11 g, 64%) {R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] = 0.13 and 0.35, respectively}, and (*S*,*S*)-*anti*- and (*R*,*S*)-*syn*-**12** (0.15 g, 62%) {R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] = 0.77} {for (*S*,*S*)-*anti*-**12**; $[\alpha]_D^{25} = -232.4$ (*c* 1.05, $CHCl_3$) and (*R*,*S*)-*syn*-**12**; $[\alpha]_D^{25} = -2.7$ (*c* 0.9, $CHCl_3$)}. These adducts were spectroscopically identical to those previously obtained.

4.1.8. Parallel kinetic resolution of oxazolidin-2-one *rac*-4 using a combination of *quasi*-enantiomeric active esters (*R*)-10 and (*S*)-13 for 2 h at −78 °C

In the same way as above, *n*-butyl lithium (0.43 ml, 2.5 M in hexane, 1.08 mmol), oxazolidin-2-one *rac*-**4** (0.145 g, 0.89 mmol), active ester (*S*)-**13** (0.20 g, 0.54 mmol) and active ester (*R*)-**10** (0.216 g, 0.54 mmol) for 2 h at −78 °C gave a crude mixture of Evans' oxazolidin-2-ones (*S*,*S*)-*anti*- and (*S*,*R*)-*syn*-**14** (ratio: 21:79). This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (7:3) to give the oxazolidin-2-one profen adducts (*S*,*R*)-*syn*- and (*S*,*S*)-*anti*-**14** (ratio 79:21; 0.192 g, 62% yield).

Characterisation data for oxazolidin-2-one (*S*,*S*)-*anti*-**14**; white solid; mp 155–158 °C; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.62; $[\alpha]_D^{25} = +156.0$ (*c* 3.5, $CHCl_3$) {for (*R*,*R*)-*anti*-**14**; $[\alpha]_D^{25} = -151.3$ (*c* 1.3, $CHCl_3$)}; $\nu_{max}(CHCl_3)$ cm^{-1} 1780 (C=O), 1701 (C=O), and 1513 (Ar); δ_H (400 MHz; $CDCl_3$) 7.39–7.23 (7H, m, 7 × CH; Ar and Ph), 7.07 (2H, d, *J* 8.2, 2 × CH, Ar), 5.33 (1H, dd, *J* 8.9 and 3.2, PhCHN), 5.10 (1H, q, *J* 7.1, ArC*H*CH$_3$), 4.55 (1H, t, *J* 8.9, C*H*$_A$H$_B$O), 4.20 (1H, dd *J* 8.9 and 3.2, CH$_A$*H*$_B$O),

2.42 (2H, d, *J* 7.2, CH_2Ar), 1.88–1.78 (1H, nonet, *J* 6.8, $CH(CH_3)_2$), 1.39 (3H, d, *J* 7.1, $ArCHCH_3$) and 0.89 (6H, d, *J* 6.7, $2 \times CH_3$; $CH_3^ACHCH_3^B$); δ_C (100.6 MHz; $CDCl_3$) 173.9 (NC=O), 153.2 (OC=O), 140.6 (*i*-C; Ar), 138.3 (*i*-C; Ar), 137.0 (*i*-C; Ph), 129.3 and 128.0 ($2 \times CH$; Ar), 128.8,[2] 128.5[1] and 125.8[2] ($5 \times CH$; Ph), 69.6 (CH_2O), 57.8 (PhCHN), 45.1 ($CH(CH_3)_2$), 43.3 ($ArCHCH_3$), 30.2 (CH_2), 22.4 (2C; $CH(CH_3)_2$) and 19.4 ($ArCHCH_3$) (Found MH^+, 352.1913; $C_{22}H_{26}NO_3$ requires 352.1907); and the oxazolidin-2-one (*S*,*R*)-*syn*-**14** as a white solid; mp 86–88 °C; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.41; $[\alpha]_D^{25} = +118.7$ (*c* 6.0, $CHCl_3$) {for (*R*,*S*)-*syn*-**14**; lit. $[\alpha]_D^{25} = -114.6$ (*c* 4.2, $CHCl_3$)}; $\nu_{max}(CHCl_3)$ cm^{-1}1779 (C=O) and 1705 (C=O); δ_H (400 MHz; $CDCl_3$) 7.28–7.15 (3H, m, $3 \times CH$; Ph), 7.00 (4H, m, $4 \times CH$, Ph and Ar), 6.90 (2H, dt, *J* 7.9 and 1.9, $2 \times CH$; Ar), 5.44 (1H, dd *J* 9.2 and 5.2, PhCHN), 5.09 (1H, q, *J* 6.9, $ArCHCH_3$), 4.63 (1H, t, *J* 9.0, CH_AH_BO), 4.06 (1H, dd, *J* 9.0 and 5.2, CH_AH_BO), 2.43 (2H, d, *J* 7.4, CH_2Ar), 1.89-1.79 (1H, nonet, *J* 6.8, $CH(CH_3)_2$), 1.38 (3H, d, *J* 6.9, $ArCHCH_3$), 0.90 (3H, d, *J* 6.6, $CH_3^ACHCH_3^B$) and 0.89 (3H, d, *J* 6.6, $CH_3^ACHCH_3^B$); δ_C (100.6 MHz; $CDCl_3$) 174.3 (NC=O), 153.3 (OC=O), 140.7 (*i*-C; Ar), 139.4 (*i*-C; Ar), 137.4 (*i*-C; Ph), 129.3[2] and 127.9[2] ($4 \times CH$; Ar), 128.8,[2] 128.5[1] and 125.8[2] ($5 \times CH$; Ph), 69.7 (CH_2O), 58.1 (PhCHN), 45.1 ($CH(CH_3)_2$), 42.7 ($ArCHCH_3$), 30.2 (CH_2Ar), 22.4[2] ($CH(CH_3)_2$) and 19.4 ($ArCHCH_3$) (Found MH^+, 352.1909; $C_{22}H_{26}NO_3$ requires MH^+, 352.1907; and found MNH_4^+, 369.2171; $C_{22}H_{29}N_2O_3$ requires MNH_4^+, 369.2173); *m*/*z* 351.1 (10% M^+), 188.1 (10, $Ar(CH_3)C{=}C{=}O^+$), 161.1 (10, Ar^+CHCH_3), 145.1 (100, $ArCH_2^+$) and 77.1 (10, Ph^+).

4.1.9. Parallel kinetic resolution of racemic oxazolidin-2-one *rac*-4 using a combination of *quasi*-enantiomeric active esters (*R*)-10 and (*S*)-13 for 2 h at rt

In the same way as above, *n*-butyl lithium (0.36 ml, 2.5 M in hexane, 0.92 mmol), oxazolidin-2-one *rac*-**4** (0.151 g, 0.92 mmol), active ester (*S*)-**13** (0.185 g, 0.46 mmol) and active ester (*R*)-**10** (0.172 g, 0.46 mmol) gave a crude mixture of oxazolidin-2-ones (*S*,*S*)-*anti*- and (*S*,*R*)-*syn*-**14** (ratio: 21:79) and (*R*,*R*)-anti- and (*R*,*S*)-*syn*-**11** (ratio: 9:91). This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (7:3) to give the profen adducts (*S*,*R*)-*syn*- and (*S*,*S*)-*anti*-**14** (ratio 79:21, 99 mg, 61%) as a colourless oil; and Mosher's adducts (*R*,*R*)-*syn*- and (*R*,*S*)-*anti*-**11** (ratio 82:18; 74 mg, 42% yield) as a colourless oil {for (*R*,*R*)-*syn*-**11**; $[\alpha]_D^{25} = +136.4$ (*c* 1.07, $CHCl_3$); and for (*R*,*S*)-*syn*-**11**; $[\alpha]_D^{25} = +22.3$ (*c* 6.1, $CHCl_3$)}. These adducts were spectroscopically identical to those previously obtained.

4.1.10. Stereospecific synthesis of 4-Phenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one (*R*,*R*)-*anti*-11

In the same way as above, *n*-butyl lithium (0.44 ml, 2.5 M in hexane, 1.10 mmol), oxazolidin-2-one (*R*)-**4** (0.15 g, 0.95 mmol) and active ester (*R*)-**10** (0.45 g, 1.12 mmol) gave a crude mixture of oxazolidin-2-one (*R*,*R*)-*anti*-**11**. This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (7:3) to give the oxazolidin-2-one (*R*,*R*)-*anti*-**11** (0.16 g, 44%) as a pale yellow oil; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.13; mp 86–88 °C; ν_{max} (CH_2Cl_2) cm^{-1} 1803 (C=O), 1702 (C=O) and 1256 (C–F); $[\alpha]_D^{22} = +136.4$ (*c* 1.07, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.34–7.13 (10H, m, $2 \times CH$; $2 \times Ph$), 5.25 (1H, dd, *J* 8.0 and 2.0, PhCHN), 4.43 (1H, dd, *J* 8.8 and 8.0, CH_AH_BO), 4.08 (1H, dd, *J* 8.8 and 2.0, CH_AH_BO) and 3.42 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 165.2 (NC=O), 149.9 (OC=O), 138.5 (*i*-C; Ph), 132.0 (*i*-C; Ph), 129.4,[1] 129.1,[3] 129.0,[1] 128.0,[2] 126.6[1] and 126.0[2] ($10 \times CH$; $2 \times Ph$), 123.2 (1C, q, $^1J_{CF}$ 290.4, CF_3), 85.7 (1C, q, $^2J_{CF}$ 26.1, $PhCCF_3$), 70.0 (CH_2O), 58.8 (PhCHN) and 56.1 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −70.7 (1C, s, CF_3) (Found MNH_4^+ 397.1370. $C_{19}H_{20}F_3N_2O_4$ requires MNH_4^+, 379.1370).

4.1.11. 4-Phenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one (*S*,*R*)-*syn*-11

In the same way as above, *n*-butyl lithium (0.38 ml, 2.5 M in hexane, 0.96 mmol), oxazolidin-2-one (*R*)-**4** (0.13 g, 0.80 mmol) and (*R*)-Mosher's chloride (0.27 g, 0.99 mmol) gave a crude mixture of oxazolidin-2-one (*S*,*R*)-*anti*-**11**. This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (7:3) to give the oxazolidin-2-one (*S*,*R*)-*syn*-**11** (0.14 g, 48%) as a white solid; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.35; mp 173–175 °C; ν_{max} (CH_2Cl_2) cm^{-1} 1796 (C=O), 1702 (C=O) and 1262 (C–F); $[\alpha]_D^{22} = -17.4$ (*c* 1.4, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.45–7.42 (2H, m, $2 \times CH$; Ph), 7.35–7.26 (8H, m, $8 \times CH$; $2 \times Ph$), 5.50 (1H, dd, *J* 6.0 and 2.5, PhCHN), 4.55 (1H, t, *J* 6.0, CH_AH_BO), 4.22 (1H, dd, *J* 6.0 and 2.5, CH_AH_BO), 3.45 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 166.3 (NC=O), 149.7 (OC=O), 138.1 (*i*-C; Ph), 131.8 (*i*-C; Ph), 129.3,[1] 129.2,[3] 129.0,[1] 127.6,[2] 126.6[1] and 126.5[2] ($10 \times CH$; $2 \times Ph$), 123.3 (1C, q, $^1J_{CF}$ 291.3, CF_3), 85.6 (1C, q, $^2J_{CF}$ 26.2, $PhCCF_3$), 69.9 (CH_2O), 58.7 (PhCHN) and 56.0 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −71.0 (1C, s, CF_3) (Found MNH_4^+ 397.1372. $C_{19}H_{20}F_3N_2O_4$ requires MNH_4^+, 379.1370).

4.1.12. 4-Phenyl-5,5-diphenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one (*R*,*S*)-*syn*-12

In the same way as above, *n*-butyl lithium (0.30 ml, 2.5 M in hexane, 0.75 mmol), oxazolidin-2-one (*S*)-**9** (0.21 g, 0.66 mmol), and active ester (*R*)-**11** (0.31 g, 0.78 mmol) gave a crude mixture of oxazolidin-2-one (*R*,*S*)-*syn*-**12**. This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (8:2) to give the oxazolidin-2-one (*R*,*S*)-*syn*-**12** (0.12 g, 34%) as a white solid; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.77; mp 199–201 °C; ν_{max} (CH_2Cl_2) cm^{-1} 1792 (C=O), 1715 (C=O) and 1267 (C–F); $[\alpha]_D^{22} = -2.7$ (*c* 0.9, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.53–7.47 (2H, m, $2 \times CH$; Ph), 7.40-7.30 (4H, m, $4 \times CH$, $2 \times Ph$), 7.10 (1H, t, *J* 7.3, CH; Ph), 7.05–6.85 (13H, m, $13 \times CH$; $4 \times Ph$), 6.23 (1H, s, PhCHN) and 3.35 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 165.6 (NC=O), 149.0 (OC=O), 141.7, 137.2, 135.1 and 131.4 ($4 \times i$-C; Ph), 129.0,[2] 128.9,[1] 128.8,[1] 128.4,[1] 128.3,[2] 127.8,[2] 127.7,[2] 127.6,[2] 127.5,[2] 126.4,[1] 125.9[2] and 125.5[2] ($20 \times CH$; $4 \times Ph$), 123.3 (1C, q, $^1J_{CF}$ 290.4, CF_3), 89.2 ($C(Ph)_2O$), 85.4 (1C, $^2J_{CF}$ 25.4, PhC), 67.6 (PhCHN) and 56.0 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −71.7 (1C, s, CF_3) (Found MNa^+ 554.1548. $C_{31}H_{24}F_3NO_4Na$ requires MNa^+, 554.1550).

4.1.13. (*S*,*S*)-4-Phenyl-5,5-diphenyl-3-(2-methoxy-2-phenyl-2-trifluoromethyl-acetyl)-oxazolidin-2-one *anti*-12

In the same way as above, *n*-butyl lithium (0.30 ml, 2.5 M in hexane, 0.75 mmol), oxazolidin-2-one (*S*)-**9** (0.21 g, 0.66 mmol) and active ester (*S*)-**10** (0.31 g, 0.78 mmol) gave a crude mixture of oxazolidin-2-one *anti*-**12**. This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (8:2) to give the oxazolidin-2-one (*R*,*S*)-*anti*-**12** (0.15 g, 43%) as a white solid; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.77; mp 151–154 °C; ν_{max} (CH_2Cl_2) cm^{-1} 1807 (C=O), 1702 (C=O) and 1256 (C–F); $[\alpha]_D^{22} = -232.4$ (*c* 1.05, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.52 (2H, d, *J* 7.4, $2 \times CH$; Ph), 7.35-7.18 (8H, m, $8 \times CH$, $2 \times Ph$), 7.09–7.05 (3H, m, $3 \times CH$, $2 \times Ph$), 6.95 (7H, m, $7 \times CH$; $3 \times Ph$), 6.00 (1H, s, PhCHN) and 2.92 (3H, s, CH_3O); δ_C (100 MHz, $CDCl_3$) 165.3 (NC=O), 149.0 (OC=O), 141.2, 136.9, 134.8 and 132.1 ($4 \times i$-C; Ph), 129.3,[1] 129.0,[2] 128.8,[1] 128.5,[1] 128.3,[2] 128.0,[2] 127.7,[2] 127.6,[1] 127.4,[2] 126.5,[2] 125.8[2] and 125.5[2] ($20 \times CH$; $4 \times Ph$), 123.1 (1C, q, $^1J_{CF}$

290.5, CF_3), 89.1 ($C(Ph)_2O$), 85.6 (1C, $^2J_{CF}$ 25.4, PhC), 67.7 (PhCHN) and 55.3 (1C, d, $^4J_{CF}$ 2.3, CH_3O); δ_F (378 MHz, $CDCl_3$) −70.3 (1C, s, CF_3) (Found MH^+ 532.1732. $C_{31}H_{25}F_3NO_4$ requires MH^+, 532.1732).

4.1.14. Hydrolysis of oxazolidin-2-one (*S,R*)-*syn*-11; synthesis of 2-methoxy-2-phenyl-2-trifluoromethyl acetic acid (*S*)-8

Lithium hydroxide monohydrate (11 mg, 0.26 mmol) was slowly added to a stirred solution of oxazolidin-2-one (*S,R*)-*syn*-**11** (50 mg, 0.13 mmol) and hydrogen peroxide (9 mg, 0.07 ml, 0.26 mmol, 3.53 M in H_2O) in THF/water (1:1; 5 ml). The reaction mixture was stirred at room temperature for 12 h. The reaction was quenched with water (10 ml) and extracted with dichloromethane (3 × 10 ml). The combined organic layers were dried (over $MgSO_4$) and evaporated under reduced pressure and purified by column chromatography to give oxazolidin-2-one (*R*)-**4** (1 mg, ~5%); R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.27; and amide (*S,R*)-**15** (37 mg, 80%) as a white solid; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.50; mp 160–163 °C; $[\alpha]_D^{20} = -42.8$ (*c* 1.1, EtOH); $\nu_{max}(CHCl_3)$ cm^{-1} 3020 (OH and NH), 1782 (C=O) and 1701 (C=O); δ_H (400 MHz; $CDCl_3$) 7.51–7.48 (3H, m, 3 × CH; 2 × Ph), 7.40–7.19 (9H, m, 7 × CH (2 × Ph), OH and NH), 5.06 (1H, dt, *J* 7.7 and 4.9, PhCHN), 3.86–3.78 (2H, dABq, C*H*$_2$OH) and 3.31 (3H, s, CH_3O); δ_C (100 MHz; $CDCl_3$) 166.7 (C=O), 138.1 and 132.2 (2 × *i*-C; Ph), 129.6,[1] 128.9,[2] 128.8,[2] 128.0,[1] 127.8,[2] and 126.6[2] (10 × CH; 2 × Ph), 123.8 (1C, q, $^1J_{C,F}$ = 288, CF_3), 84.2 (1C, q, $^1J_{C,F}$ = 24.7, PhC), 66.1 (CH_2O), 55.5 (CH_3O) and 54.9 (PhCHN); δ_F (378 MHz, $CDCl_3$) −70.1 (1C, s, CF_3) (Found MH^+ 354.1310. $C_{18}H_{19}F_3O_3N^+$ requires MH^+, 354.1312). The aqueous phase was acidified using HCl (3 M HCl) until the pH 3, extracted with diethyl ether (3 × 10 ml). The combined organic phases were dried (over $MgSO_4$) and evaporated under reduced pressure to give (−)-2-methoxy-2-phenyl-2-trifluoromethyl acetic acid (*S*)-**8** (~2 mg, 6%) as an oil; >95% ee;[28] $[\alpha]_D^{20}$ = −65.0 (*c* 0.4, $CHCl_3$) {lit.[29] $[\alpha]_D^{22} = -71.6$ (*c* 0.23, EtOH); lit.[30] $[\alpha]_D$ = −69.0 (*c* 1.13, MeOH); lit.[31] $[\alpha]_D$ = −69.5 (*c* 1.2, MeOH)}; $\nu_{max}(CHCl_3)$ cm^{-1} 3015 (OH), 1785w (C=O) and 1729 (C=O), δ_H (400 MHz; $CDCl_3$) 7.58–7.57 (2H, m, 2 × CH; Ph), 7.45–7.37 (3H, m, 3 × CH; Ph), 6.37 (1H, br s, OH) and 3.53 (3H, s, CH_3O); δ_C (100 MHz; $CDCl_3$) 166.9 (C=O), 131.2 (*i*-C; Ph), 129.9,[1] 128.6,[2] and 127.3[2] (5 × CH; Ph), 125.6 (1C, q, $^1J_{C,F}$ = 289 Hz, CF_3), 88.2 (1C, q, $^1J_{C,F}$ = 27.5, PhC) and 55.1 (CH_3O) (Found MNH_4^+ 252.0844. $C_{10}H_{13}F_3NO_3$ requires MNH_4^+, 252.0842).

4.1.15. Hydrolysis of oxazolidin-2-one (*R,S*)-*syn*-12; synthesis of 2-methoxy-2-phenyl-2-trifluoromethyl acetic acid (*R*)-8

In the same way as above, 2-methoxy-2-phenyl-2-trifluoromethyl acetic acid (*S*)-**8**, oxazolidin-2-one (*R,S*)-*syn*-**12** (49 mg, 92 μmol), lithium hydroxide monohydrate (8 mg, 0.18 mmol) and hydrogen peroxide (6 mg, 0.05 ml, 0.18 mmol, 3.53 M in H_2O) in THF/water (1:1; 5 ml) gave after purification by aqueous extraction (+)-2-methoxy-2-phenyl-2-trifluoromethyl acetic acid (*R*)-**8** (10 mg, 46%) as a liquid; $[\alpha]_D^{22} = +67.0$ (*c* 0.6, $CHCl_3$) {lit.[29] $[\alpha]_D$ = +69.8 (*c* 0.22, EtOH)}, which was spectroscopically identical to those previously obtained. The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure and purified by column chromatography to give the 4,5,5-triphenyl-oxazolidin-2-one (*S*)-**9** (5 mg, 17%); R_F [light petroleum ether (bp 40-60 °C)/diethyl ether (1:1)] 0.13; and the amide (*S,R*)-**16** (11 mg, 24%) as a white solid; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.41; mp 156–160 °C; $[\alpha]_D^{20} = -132.0$ (*c* 1.6, $CHCl_3$); $\nu_{max}(CHCl_3)$ cm^{-1} 1781 (C=O) and 1704 (C=O); δ_H (400 MHz; $CDCl_3$) 7.86 (1H, br d, *J* 9.1, NH), 7.50 (2H, dt, *J* 6.7 and 1.6, 2 × CH; Ph), 7.28–7.20 (3H, m, 3 × CH; 2 × Ph), 7.20–7.14 (4H, m, 4 × CH; 2 × Ph), 7.14–7.05 (6H, m, 6 × CH; 2 × Ph), 7.05–6.99 (5H, m, 5 × CH; 2 × Ph), 6.01 (1H, d, *J* 9.1, PhCHN), 3.05 (3H, s, CH_3O) and 2.58 (1H, s, OH); δ_C (100 MHz; $CDCl_3$) 165.1 (C=O), 143.9, 143.7, 136.8 and 131.7 (4 × *i*-C; 4 × Ph), 129.1,[1] 128.5,[4] 128.4,[2] 128.1,[2] 127.9,[2] 128.8,[2] 127.7,[1] 127.2,[1] 127.1,[1] 125.8,[2] and 125.4,[2] (20 × CH; 4 × Ph), 123.7 (1C, q, $^1J_{C,F}$ = 289, CF_3), 83.9 (1C, q, $^1J_{C,F}$ = 26.1, PhC), 80.8 (CPh_2) 58.8 (CH_3O) and 54.7 (PhCHN); δ_F (378 MHz, $CDCl_3$) −69.1 (1C, s, CF_3) (Found MNH_4^+ 252.0844. $C_{10}H_{13}F_3NO_3$ requires MNH_4^+, 252.0842).

4.1.16. Hydrolysis of oxazolidin-2-one (*R,S*)-*syn*-12 with 24% de

In the same way as above, oxazolidin-2-one (*R,S*)-*syn*-**12** (24% de) (0.15 g, 0.28 mmol), lithium hydroxide monohydrate (24 mg, 0.54 mmol) and hydrogen peroxide (18 mg, 0.15 ml, 0.54 mmol, 3.53 M in H_2O) in THF/water (1:1; 5 ml) gave after purification by aqueous extraction 2-methoxy-2-phenyl-2-trifluoromethyl acetic acid (+)-(*R*)-**8** (17 mg, 26%) as a liquid; ~24% ee;[28] $[\alpha]_D^{22} = +16.9$ (*c* 3.4, $CHCl_3$) {lit.[29] $[\alpha]_D$ = +69.8 (*c* 0.22, EtOH)}, which was spectroscopically identical to that previously obtained.

4.1.17. Characterisation data for the formation of amide (*R,R*)-*anti*-17 [derived from *n*-BuOLi addition to oxazolidin-2-one (*R,R*)-*anti*-11]

Colourless oil; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.5; $[\alpha]_D^{22} = -24.75$ (*c* 3.2, $CHCl_3$); $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1742 (C=O) and 1702 (C=O); δ_H (400 MHz, $CDCl_3$) 7.37–7.32 (2H, m, 2 × CH; Ph), 7.31–7.21 (6H, m, 6 × CH; 2 × Ph), 7.16–7.11 (2H, m, 2 × CH; Ph), 5.27 (1H, td, *J* 7.6 and 3.4, PhCHN), 4.34 (2H, dABq, *J* 7.6 and 11.6, CH_2O), 4.07 (2H, td, *J* 6.8 and 3.2, CH_2O; OBu), 3.40 (3H, s, CH_3O), 1.56 (2H, appears as a quintet, *J* 6.7, CH_2), 1.31 (2H, appears as a sextet, *J* 7.5, CH_2) and 0.85 (3H, t, *J* 7.3, C*H*$_3$CH$_2$); δ_C (100 MHz, $CDCl_3$) 166.2 (NC=O), 155.3 (OC=O), 137.1 (*i*-C; Ph), 132.3 (*i*-C; Ph), 129.5,[1] 128.8,[2] 128.4,[2] 128.2,[1] 127.5[2] and 126.7[2] (10 × CH; 2 × Ph), 123.9 (1C, q, $^1J_{CF}$ 288.7, CF_3), 84.0 (1C, q, $^2J_{CF}$ 25.9, PhC*C*F$_3$), 68.6 (CH_2O), 68.4 (CH_2O), 55.1 (PhCHN), 52.7 (OCH_3), 30.5 (CH_2), 18.8 (CH_2) and 13.6 (CH_3); δ_F (378 MHz, $CDCl_3$) −68.8 (1C, s, CF_3) (Found MH^+ 454.1837. $C_{23}H_{27}F_3NO_5$ requires MH^+, 454.1836).

4.1.18. Characterisation data for the formation of amide (*S,R*)-*syn*-17 [derived from *n*-BuOLi addition to oxazolidin-2-one (*S,R*)-*syn*-11]

Colourless oil; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.5; $[\alpha]_D^{22} = -19.2$ (*c* 3.9, $CHCl_3$); $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1742 (C=O) and 1702 (C=O); δ_H (400 MHz, $CDCl_3$) 7.55–7.51 (2H, m, 2 × CH; Ph), 7.39–7.36 (4H, m, 4 × CH; 2 × Ph), 7.35–7.33 (2H, m, 2 × CH; Ph), 7.32–7.29 (2H, m, 2 × CH; Ph), 5.27 (1H, dt, *J* 8.4 and 6.0, PhCHN), 4.38 (2H, d, *J* 6.0, CH_2O), 4.08 (2H, td, *J* 6.8 and 3.8, CH_2O; OBu), 3.36 (3H, s, CH_3O), 1.59 (2H, appears as a quintet, *J* 6.7, CH_2), 1.35 (2H, appears as a sextet, *J* 7.3, CH_2) and 0.85 (3H, t, *J* 7.3, C*H*$_3$CH$_2$); δ_C (100 MHz, $CDCl_3$) 166.2 (NC=O), 155.3 (OC=O), 137.2 (*i*-C; Ph), 132.3 (*i*-C; Ph), 129.5,[1] 128.9,[2] 128.5,[2] 128.2,[1] 127.8[2] and 126.6[2] (10 × CH; 2 × Ph), 123.7 (1C, q, $^1J_{CF}$ 288.3, CF_3), 84.1 (1C, q, $^2J_{CF}$ 26.8, PhC*C*F$_3$), 68.7 (CH_2O), 68.3 (CH_2O), 54.9 (PhCHN), 52.5 (OCH_3), 30.6 (CH_2), 18.8 (CH_2) and 13.6 (CH_3); δ_F (378 MHz, $CDCl_3$) −68.7 (1C, s, CF_3) (Found MH^+ 454.1835. $C_{23}H_{27}F_3NO_5$ requires MH^+, 454.1836).

4.1.19. Characterisation data for the formation of amides (*RS,RS*)-*anti*- and (*RS,SR*)-*syn*-17 [derived from *n*-BuOLi addition to oxazolidin-2-ones (*RS,RS*)-*anti*- and (*RS,SR*)-*syn*-11 ratio (21:79)]

Amide (*RS,RS*)-*anti*- and (*RS,SR*)-*syn*-**17** (ratio: 21:79); colourless oil; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.5; $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1743 (C=O) and 1700 (C=O); δ_H (400 MHz, $CDCl_3$) 7.51–7.45 (2H, m, 2 × CH; Ph^S), 7.40–7.20 (16H, m, 16 2 × CH; 2 × Ph^{S+A}), 7.15–7.11 (2H, m, 2 × CH; Ph^A), 5.27 (1H, td, *J* 7.6 and 3.4, PhCHN^{S+A}), 4.34 (4H, dABq, *J* 7.6 and 11.6, CH_2O^{S+A}),

4.07 (2H, td, *J* 6.8 and 3.2, CH_2O; OBu^A), 3.95 (2H, td, *J* 6.8 and 3.2, CH_2O; OBu^S), 3.40 (3H, s, CH_3O^A), 3.31 (3H, s, CH_3O^S), 1.60–1.50 (4H, m, CH_2^{S+A}), 1.31 (4H, m, CH_2^{S+A}), 0.86 (3H, t, *J* 7.3, $CH_3CH_2^A$) and 0.85 (3H, t, *J* 7.3, $CH_3CH_2^S$); δ_C (100 MHz, $CDCl_3$) 166.2 (2C; $NC{=}O^{S+A}$), 155.3 (2C; $OC{=}O^{S+A}$), 137.1 (2C; *i*-C; Ph^{S+A}), 132.3 (*i*-C; Ph^A), 132.2 (*i*-C; Ph^S), 129.5^S,[1] 129.4^A,[1]128.9^S,[2] 128.8^A,[2] 128.5^S,[2] 128.4^A,[2] 128.2^A,[1] 128.1^S,[1] 127.8^S,[2] 127.5^A,[2] 126.7^S,[2] and 126.6^A,[2] (20 × CH; 2 × Ph^{S+A}), 123.7 (1C, q, $^1J_{CF}$ 289.5, CF_3^S), 123.6 (1C, q, $^1J_{CF}$ 288.7, CF_3^A), 84.1 (1C, q, $^2J_{CF}$ 25.9, $PhCCF_3^S$), 84.0 (1C, q, $^2J_{CF}$ 25.9, $PhCCF_3^A$), 68.7 (CH_2O^S), 68.6 (CH_2O^A), 68.3 (CH_2O^S), 68.3 (CH_2O^A), 55.1 ($PhCHN^A$), 54.9 ($PhCHN^S$), 52.7 (OCH_3^A), 52.5 (OCH_3^S), 30.5 (2C; CH_2^{S+A}), 18.8 (2 C; CH_2^{S+A}), 13.6 (CH_3^S) and 13.6 (CH_3^A); δ_F (378 MHz, $CDCl_3$) −68.8 (1C, s, CF_3^A) and −68.7 (1C, s, CF_3^S) (Found MH^+ 454.1835. $C_{23}H_{27}F_3NO_5$ requires MH^+, 454.1836).

4.1.20. Characterisation data for (*R*)-butyl 2-methoxy-2-phenyl-2-trifluoromethyl acetate 8

Colourless oil; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.76; $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1747 (C=O); $[\alpha]_D^{22} = +48.0$ (*c* 5.8, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.51–7.45 (2H, m, 2 × CH; Ph^S), 7.53–7.48 (2H, m, 2 × CH; Ph), 7.41–7.36 (3H, m, 3 × CH; Ph), 4.36–4.25 (2H, m, CH_2O), 3.53 (3H, q, $^4J_{CF}$ 1.1, OCH_3), 1.70–1.62 (2H, m, CH_2), 1.39–1.30 (2H, appears as a br sextet, *J* 7.3, CH_2) and 0.89 (3H, t, *J* 7.5, CH_3CH_2); δ_C (100 MHz, $CDCl_3$) 166.5 (C=O), 132.3 (*i*-C; Ph), 129.5,[1] 128.3[2] and 127.2[2] (5 × CH; Ph), 124.1 (1C, q, $^1J_{CF}$ 286.5, CF_3), 84.5 (1C, q, $^2J_{CF}$ 26.7, $PhCCF_3$), 66.2 (CH_2O), 55.3 (OCH_3), 30.3 (CH_2), 18.9 (CH_2) and 13.4 (CH_3); δ_F (378 MHz, $CDCl_3$) −71.5 (1C, s, CF_3); (Found MNH_4^+ 308.1467. $C_{14}H_{21}F_3NO_3$ requires MNH_4^+, 308.1468).

4.1.21. Synthesis of (2*S*,4*R*)-*N*-(2-hydroxy-1-phenylethyl)-2-phenyl-2-methoxy-2-trifluoromethylacetamide (*S*,*R*)-*syn*-15 (using 3 equiv of *n*-BuLi)

In the same way as above, *n*-butyl lithium (70 μl, 2.5 M in hexane, 0.18 mmol), butanol (22 mg, 0.30 mmol) and oxazolidin-2-one (*S*,*R*)-*syn*-**11** (23 mg, 60 μmol) gave a crude mixture of amide (*S*,*R*)-*syn*-**15**. This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (7:3→3:7) to give the amide (*S*,*R*)-*syn*-**15** (9 mg, 42%) as a white solid (mp 160–163 °C), which was spectroscopically identical to that previously obtained.

4.1.22. Synthesis of (2*R*,2*S*)-(2-phenyl-2-methoxy-2-trifluoroethanonyl){2-[(butoxycarbonyl)oxy]-2,2-diphenyl-2-phenylethyl} carbamate (*R*,*S*)-*syn*-18 (using 1 equiv of *n*-BuLi)

In the same way as above, *n*-butyl lithium (0.20 ml, 2.5 M in hexane, 0.50 mmol), butanol (33 mg, 0.45 mmol) and oxazolidin-2-one (*R*,*S*)-*syn*-**12** (0.17 g, 0.45 mmol) gave a crude mixture of amides and (*R*,*S*)-*syn*-**16** and (*R*,*S*)-*syn*-**18** (ratio 11:89). This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (9:1→3:7) to give the amide (*R*,*S*)-*syn*-**18** (48 mg, 23%) as a colourless oil; R_F [light petroleum ether (bp 40–60 °C)/diethyl ether (1:1)] 0.58; {$[\alpha]_D^{22} = -48.3$ (*c* 6.2, $CHCl_3$) [for a ratio 89:11 of (*R*,*S*)-*syn*-**18**:(*R*,*S*)-*syn*-**12**]}; $\nu_{max}(CH_2Cl_2)$ cm^{-1} 1740 (C=O) and 1709 (C=O); δ_H (400 MHz, $CDCl_3$) 8.90 (1H, br s, NH), 7.55 (2H, br d, *J* 7.1, 2 × CH; Ph), 7.45–7.35 (3H, m, 4 × CH; 2 × Ph), 7.28–7.14 (11H, m, 2 × CH; Ph), 7.05 (2H, br d, *J* 7.1, 2 × CH; Ph), 6.76 (2H, br d, *J* 7.1, 2 × CH; Ph), 6.28 (1H, d, *J* 9.1, PhCH), 4.14 (2H, td, *J* 6.6 and 1.8, CH_2O; OBu), 3.28 (3H, s, CH_3O), 1.64 (2H, appears as a quintet, *J* 6.6, CH_2), 1.39 (2H, appears as a sextet, *J* 7.3, CH_2) and 0.94 (3H, t, *J* 7.3, CH_3CH_2); δ_C (100 MHz, $CDCl_3$) 165.2 (NC=O), 154.1 (OC=O), 141.5, 139.6, 136.5 and 132.4 (4 × *i*-C; 4 × Ph), 129.3,[1] 128.5,[2] 128.4,[2] 128.1,[2] 127.9,[1] 127.8,[5] 127.7,[1] 127.5,[2] 127.3[2] and 127.0[2] (20 × CH; 4 × Ph), 123.6 (1C, q, $^1J_{C,F} = 288$, CF_3), 89.1 (CPh_2), 83.4 (1C, q, $^1J_{C,F} = 25.2$, $PhCCF_3$), 68.3 (CH_2O), 57.9 (PhCHN), 55.1 (CH_3O), 30.6 (CH_2), 18.7 (CH_2) and 13.6 (CH_3); δ_F (378 MHz, $CDCl_3$) −69.0 (1C, s, CF_3) (Found MH^+ 606.2465. $C_{35}H_{35}F_3NO_5$ requires MH^+, 606.2462); and the amide (*R*,*S*)-*syn*-**16** (4 mg, 3%) as a colourless oil, which was spectroscopically identical to that previously obtained.

4.1.23. Synthesis of (2*R*,2*S*)-(2-phenyl-2-methoxy-2-trifluoroethanonyl){2-[(butoxycarbonyl)oxy]-2,2-diphenyl-2-phenylethyl} carbamate (*R*,*S*)-*syn*-18 (using 3 equiv of *n*-BuLi)

In the same way as above, *n*-butyl lithium (0.41 ml, 2.5 M in hexane, 1.03 mmol), butanol (0.127 g, 1.71 mmol) and oxazolidin-2-one (*R*,*S*)-*syn*-**12** (0.13 g, 0.34 mmol) gave a crude mixture of amides (*R*,*S*)-*syn*-**16** and (*R*,*S*)-*syn*-**18** (ratio 23:77). This residue was purified by flash column chromatography eluting with light petroleum ether (bp 40–60 °C)/diethyl ether (9:1→3:7) to give the amides (*R*,*S*)-*anti*-**16** (4 mg, 3%) and (*R*,*S*)-*anti*-**18** (42 mg, 27%) as colourless oils, both of which were spectroscopically identical to that previously obtained.

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References

1. (a) Alper, H.; Hamel, N. *J. Am. Chem. Soc.* **1990**, *112*, 2803–2804; (b) Piccolo, O.; Spreafico, F.; Visentin, G.; Valoti, E. *J. Org. Chem.* **1985**, *50*, 3945–3946; (c) Piccolo, O.; Azzena, U.; Melloni, G.; Delogu, G.; Valoti, E. *J. Org. Chem.* **1991**, *56*, 183–187; (d) Ohta, T.; Takaya, H.; Kitamura, M.; Nagai, K.; Noyori, R. *J. Org. Chem.* **1987**, *52*, 3174–3176; (e) Stille, J. K.; Parrinello, G. *J. Mol. Catal.* **1983**, *21*, 203–210; (f) Kumar, A.; Salunkhe, R. V.; Rane, R. A.; Dike, S. Y. *J. Chem. Soc., Chem. Commun.* **1991**, 485–486; (g) Franck, A.; Ruchardt, C. *Chem. Lett.* **1984**, 1431–1434; (h) Prasad, K. R.; Chandrakumar, A. *Tetrahedron: Asymmetry* **2005**, *16*, 1897–1900; (i) Moreno-Dorado, F. J.; Guerra, F. M.; Ortega, M. J.; Zubia, E.; Massanet, G. M. *Tetrahedron: Asymmetry* **2003**, *14*, 503–510.
2. (a) Sonawane, H. R.; Bellur, N. S.; Ahuja, J. R.; Kulkarni, D. G. *Tetrahedron: Asymmetry* **1992**, *3*, 163–192; (b) Fuji, K.; Node, M.; Tanaka, F.; Hosoi, S. *Tetrahedron Lett.* **1989**, *30*, 2825–2828; (c) Corriu, J. P.; Masse, J. P. *J. Chem. Soc., Chem. Commun.* **1972**, 144–145; (d) Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 4374–4379; (e) Hayashi, T.; Konishi, M.; Fukushima, M.; Kanehira, K.; Hioki, T.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 2195–2202; (f) Larsen, R. D.; Corley, E. G.; Davis, P.; Reider, P. J.; Grabowski, E. J. J. *J. Am. Chem. Soc.* **1989**, *111*, 7650–7651.
3. (a) Huang, H.-R.; Xu, J.-H.; Xu, Y.; Pan, J.; Liu, X. *Tetrahedron: Asymmetry* **2005**, *16*, 2113–2117; (b) Tanaka, K.; Fukuoka, T.; Shiro, M. *J. Chem. Res. (S)* **2002**, 446–447; (c) Mateo, C.; Chmura, A.; Rustler, S.; van Rantwijk, F.; Stolz, A.; Sheldon, R. A. *Tetrahedron: Asymmetry* **2006**, *17*, 320–323; (d) Bew, S. P.; Davies, S. G.; Fukuzawa, S.-I. *Chirality* **2000**, *12*, 483–487.
4. Nerurkar, S. G.; Dighe, S. V.; Williams, R. L. *J. Clin. Pharmacol.* **1992**, *32*, 935–943.
5. For some recent examples, see: (a) Blay, G.; Fernandez, I.; Monje, B.; Munoz, M. C.; Pedro, J. R.; Vila, C. *Tetrahedron* **2006**, *62*, 9174–9182; (b) Blay, G.; Fernandez, I.; Monje, B.; Munoz, M. C.; Pedro, J. R.; Vila, C. *Tetrahedron* **2006**, *62*, 8069–8076; (c) Lee, Y. J.; Lee, K.; Jung, S. I.; Jeon, H. B.; Kim, K. S. *Tetrahedron* **2005**, *61*, 1987–2001.
6. For reviews see: (a) Eames, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 885–888; (b) Eames, J.. In *Organic Synthesis Highlights*; VCH-Wiley, 2003; Vol. v, Chapter 17. pp 151–164; (c) Dehli, J. R.; Gotor, V. *Chem. Soc. Rev.* **2002**, *31*, 365–370; (d) Dehli, J. R.; Gotor, V. *ARKIVOC* **2002**, *v*, 196–202.
7. Coumbarides, G. S.; Dingjan, M.; Eames, J.; Flinn, A.; Northen, J.; Yohannes, Y. *Tetrahedron Lett.* **2005**, *46*, 2897–2902.
8. Coumbarides, G. S.; Dingjan, M.; Eames, J.; Flinn, A.; Motevalli, M.; Northen, J.; Yohannes, Y. *Synlett* **2006**, 101–105.
9. (a) Coumbarides, G. S.; Dingjan, M.; Eames, J.; Flinn, A.; Northen, J. *Chirality* **2007**, *19*, 321–328; (b) Chavda, S.; Coumbarides, G. S.; Dingjan, M.; Eames, J.; Flinn, A.; Northen, J. *Chirality* **2007**, *19*, 313–320.
10. Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.
11. (a) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737–1739; (b) Evans, D. A. *Aldrichim. Acta* **1982**, *15*, 23–32; (c) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127–2129.
12. (a) Hintermann, T.; Seebach, D. *Helv. Chim. Acta* **1998**, *81*, 2093–2126; (b) Gaul, C.; Schweizer, B.; Seiler, P.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 1546–1566.

13. The (*R*)- and (*S*)-enantiomer of active ester **10** can be synthesised in 92% and 88%, respectively.
14. The data relating to the single crystal X-ray structures of (*R*)-**10** has been deposited at the Cambridge Crystallographic Database {CCDC reference number 683188}.
15. The absolute configurations of each diastereoisomer were assigned by stereospecific synthesis; see Section 4 for details.
16. Eames, J.; Boyd, E.; Chavda, S.; Eames, J.; Yohannes, Y. *Tetrahedron: Asymmetry* **2007**, *18*, 476–482.
17. The configurational assignment was determined through stereospecific synthesis.
18. Boyd, E.; Chavda, S.; Coulbeck, E.; Coumbarides, G. S.; Dingjan, M.; Eames, J.; Flinn, A.; Motevalli, M.; Northen, J.; Yohannes, Y. *Tetrahedron: Asymmetry* **2007**, *18*, 2515–2530.
19. An equimolar amount of (*R*)-**4**-Li and *rac*-**13** gave the corresponding adduct (*S*,*R*)-*syn*-**14** in 48% yield with 60% de (reported in Yohannes, Y. PhD Thesis, University of London, 2004).
20. The relative rate difference must be at least two orders of magnitude as determined by ^{1}H NMR spectroscopy.
21. (a) Kroutil, W.; Kleewein, A.; Faber, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3263–3274; (b) Majeric, M.; Sunjic, V. *Tetrahedron: Asymmetry* **1996**, *7*, 815–824; (c) Caron, G.; Kazlauskas, R. J. *Tetrahedron: Asymmetry* **1993**, *4*, 1995–2000; (d) Brown, S. M.; Davies, S. G.; Desousa, J. A. A. *Tetrahedron: Asymmetry* **1993**, *4*, 813–822; (e) Brown, S. M.; Davies, S. G.; Desousa, J. A. A. *Tetrahedron: Asymmetry* **1991**, *2*, 511–514; (f) Chen, C. S.; Liu, Y. C. *J. Org. Chem.* **1991**, *56*, 1966–1968; (g) Schreiber, S. L.; Schreiber, T. S.; Smith, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 1525–1529.
22. The low recoverability of the oxazolidinone (*S*)-**9** was due to its insoluble nature.
23. (a) Davies, S. G.; Doisneau, G. J.-M.; Prodger, J. C.; Sanganee, H. J. *Tetrahedron Lett.* **1994**, *35*, 2369–2372; (b) Davies, S. G.; Doisneau, G. J.-M.; Prodger, J. C.; Sanganee, H. J. *Tetrahedron Lett.* **1994**, *35*, 2373–2376; (c) Davies, S. G.; Sanganee, H. J. *Tetrahedron: Asymmetry* **1995**, *6*, 671–674.
24. For a comprehensive account of *endo*-cleavage of 4-alkyl substituted-5,5-dimethyl-oxazolidin-2-ones (known as SuperQuats) see: (a) Davies, S. G.; Hunter, I. A.; Nicholson, R. L.; Roberts, P. M.; Savory, E. D.; Smith, A. D. *Tetrahedron: Asymmetry* **2004**, *60*, 7553–7577; (b) Davies, S. G.; Nicholson, R. L.; Smith, A. D. *Org. Biomol. Chem.* **2004**, *2*, 3385–3400.
25. The THF solvent must be degassed with N_2 prior to use.
26. Determined by (400 MHz) ^{1}H NMR spectroscopy.
27. Campbell, J. A.; Lee, W. K.; Rapport, H. *J. Org. Chem.* **1995**, *60*, 4602–4616.
28. The enantiomeric excess was determined by DCC coupling with either (*R*)- or (*S*)-1-phenylethanol.
29. Moreno-Dorado, F. J.; Guerra, F. M.; Ortega, M. J.; Zubia, E.; Massanet, G. M. *Tetrahedron: Asymmetry* **2003**, *14*, 503–510.
30. Givens, R. S.; Chae, W. K.; Matuszewski, B. *J. Am. Chem. Soc.* **1982**, *104*, 2456–2466.
31. Benson, S. C.; Cai, P.; Colon, M.; Haiza, M. A.; Tokles, M.; Snyder, J. K. *J. Org. Chem.* **1988**, *53*, 5335–5341.