Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 18 (2007) 476–482

Parallel kinetic resolution of 2-methoxy and 2-phenoxy-substituted carboxylic acids using a combination of *quasi*-enantiomeric oxazolidinones

Ewan Boyd,[a] Sameer Chavda,[b] Jason Eames[b,*] and Yonas Yohannes[c]

[a]*Syngenta, Grangemouth Manufacturing Centre, Earls Road, Grangemouth, Scotland FX3 8X, UK*
[b]*Department of Chemistry, University of Hull, Cottingham Road, Kingston upon Hull HU6 7RX, UK*
[c]*Department of Chemistry, Queen Mary, University of London, Mile End Road, London E1 4NS, UK*

Received 4 January 2007; accepted 8 January 2007
Available online 21 February 2007

Abstract—2-Methoxy-2-phenyl acetic acid and 2-phenoxy-2-phenylpropionic acid were resolved by the parallel kinetic resolution of their corresponding pentafluorophenyl active ester using a *quasi*-enantiomeric combination of lithiated oxazolidinones.

1. Introduction

The synthesis of enantiomerically pure carboxylic acids[1] based on the carbon-skeleton of phenylacetic acid, such as 2-phenylpropionic acid,[2] mandelic acid[3] and phenylglycine[4] is well documented. Many of these derivatives have found widespread use as synthetic building blocks[5] and many of these derivatives have been shown to have biological importance.[6]

2. Results and discussion

Over the last decade, the parallel separation of enantiomers by kinetic resolution has attracted some attention.[7] This particular concept was developed by Davies[8] and Vedejs.[9] More recently, Davies[10] has shown elegantly the parallel separation of a racemic enoate (*rac*)-**1** using an equimolar combination of two *quasi*-enantiomeric lithium amides (*S*)-**2** and (*R*)-**3** to give two separable β-amino esters *syn*,*syn*,*anti*-**4** and *syn*,*syn*,*anti*-**5**, respectively, in good yields (35–39% out of a maximum of 50%) with high levels of diastereoselectivity (95–99% de) (Scheme 1).

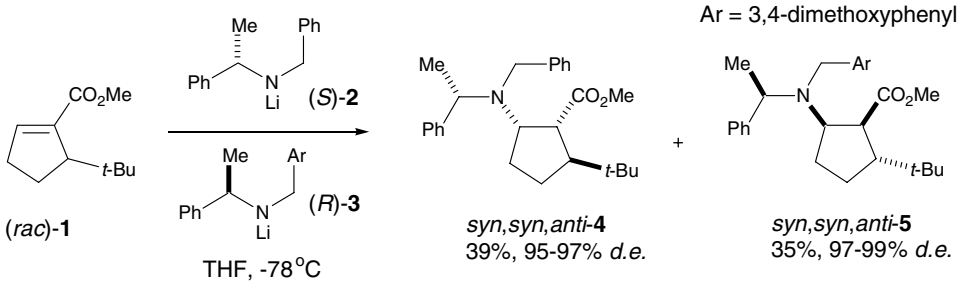
From our laboratory,[11,12] we have reported[11] the parallel kinetic resolution of pentafluorophenyl 2-phenylpropionate (*rac*)-**8** can be achieved using two lithiated *quasi*-enantiomeric Evans oxazolidinones [derived from oxazolidinone (*R*)-**6** and (*S*)-**7**] to give the corresponding *syn*-adducts **9** and **10** in good yield with high levels of diastereocontrol (Scheme 2). We have also demonstrated[12] that complementary parallel kinetic resolution of oxazolidinone (*rac*)-**6** can occur efficiently by using two complementary *quasi*-enantiomeric pentafluorophenyl active esters, (*S*)-**11** and (*R*)-**12**, to give the corresponding *syn*-adducts **13** and **14** respectively, with excellent levels of diastereoselectivity (Scheme 3).

We now report an extension to our methodology for the resolution of 2-methoxy-2-phenyl acetic acid (*rac*)-**15** and 2-phenoxy-2-phenylpropionic acid (*rac*)-**16** using a *quasi*-enantiomeric combination of Evans' oxazolidinones (Scheme 4). We chose to focus our attention on two pentafluorophenyl active esters (*rac*)-**17** and (*rac*)-**18** derived from the corresponding 2-methoxy-2-phenyl acetic acid (*rac*)-**15** and 2-phenoxy-2-phenylpropionic acid (*rac*)-**16** as these were structurally related to our original[11,12] 2-phenylpropionic acid substrate (Scheme 4). These active esters (*rac*)-**17** and (*rac*)-**18** were synthesised in moderate to good yield by the addition of DCC to a stirred solution of pentafluorophenol and the corresponding carboxylic acids (*rac*)-**15** and (*rac*)-**16**, respectively, in dichloromethane.

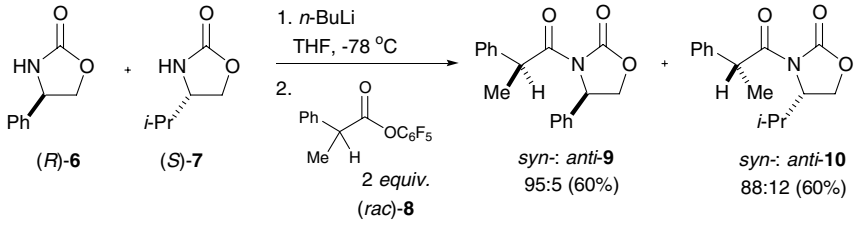
In order to determine the levels of mutual recognition between active esters (*rac*)-**17** and (*rac*)-**18**, and the associated oxazolidinones (e.g., **6** and **7**), we first screened their

* Corresponding author. Tel.: +44 1482 466401; fax: +44 1482 466410; e-mail: j.eames@hull.ac.uk

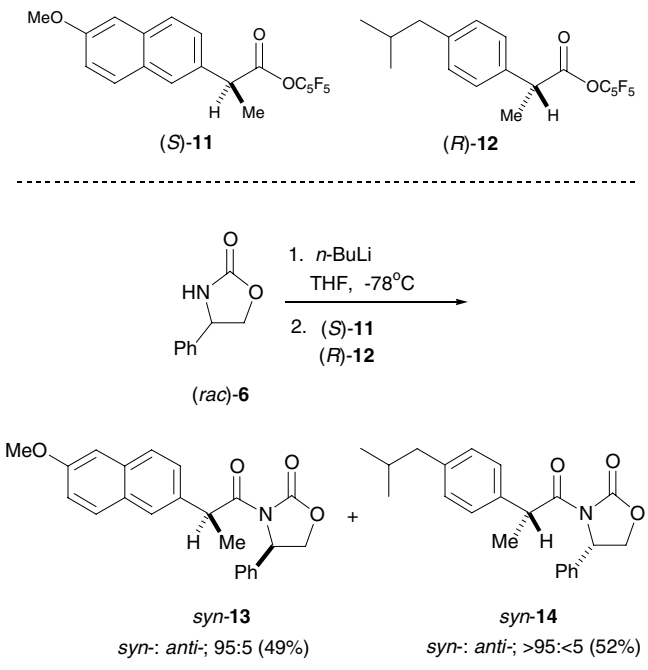
0957-4166/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2007.01.018



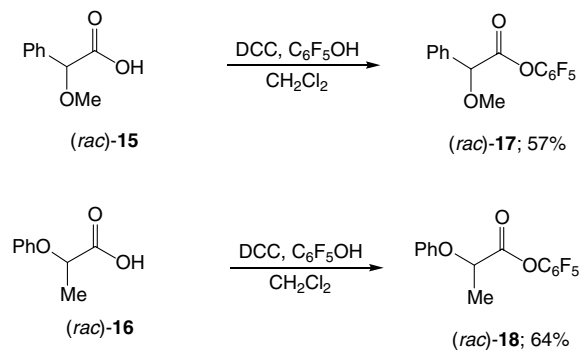
Scheme 1. Parallel kinetic resolution of enoate (*rac*)-**1**.



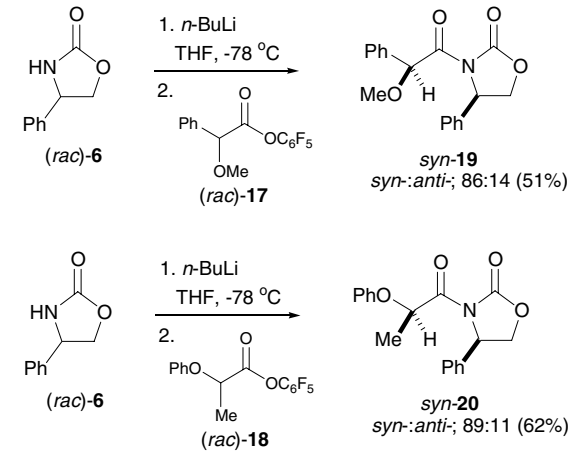
Scheme 2. Parallel kinetic resolution of active ester (*rac*)-**8**.



Scheme 3. Parallel kinetic resolution of oxazolidinone (*rac*)-**6**.



Scheme 4. Synthesis of active esters (*rac*)-**17** and (*rac*)-**18**.



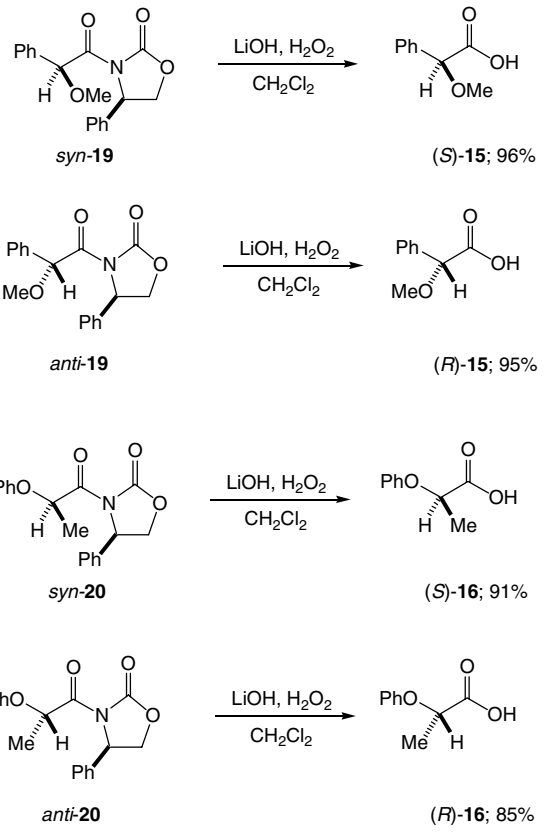
Scheme 5. Mutual kinetic resolution of active esters (*rac*)-**17** and (*rac*)-**18**.

mutual kinetic resolution using racemic oxazolidinone (*rac*)-**6** (derived from phenylglycine) as our model substrate (Scheme 5).[13] Deprotonation of oxazolidinone (*rac*)-**6** (by the addition of *n*-butyl lithium in THF at −78 °C), followed by the addition of pentafluorophenyl 2-methoxy-2-phenyl acetate (*rac*)-**17** and pentafluorophenyl 2-phenoxypropionate (*rac*)-**18**, gave the corresponding diastereoisomeric adducts **19** and **20** in good yield (Scheme 5). The levels of diastereocontrol were excellent favouring formation of the *syn*-diastereoisomeric adducts **19** and **20**, respectively (Scheme 5). The relative stereochemical outcome of these mutual kinetic resolutions appear to be similar for both active esters, (*rac*)-**17** and (*rac*)-**18**. However, it is interesting to note, their mutual enantiomer recognition processes were evidently different;[14] that is, oxazolidinone (*R*)-**6** appears to recognise (*S*)-enantiomer

of **17** but (*R*)-enantiomer of **18**, and vice versa. This is also true for their complementary mirror image combinations. From these mutual resolutions, it appears that the Lewis basicity of the oxygen atom at the C(2) position [within both active esters (*rac*)-**17** and (*rac*)-**18**] mediates the diastereoselection; the more Lewis basic OMe group promotes formation of *syn*-**19**, whereas the less Lewis basic OPh group favours the formation of *syn*-**20** (Scheme 5). It is worthy of note, that this situation is additional complicated due to the competitive Lewis basicity of the pentafluorophenyl *pro*-leaving group.

With this information in hand, we next probed the parallel kinetic resolution of these racemic active esters (*rac*)-**17** and (*rac*)-**18** using an equimolar combination of lithiated oxazolidinones. For this study, we chose to use the combination of oxazolidinone, (*R*)-**6**, and its complementary *quasi*-enantiomer, (*S*)-**7**, as our parallel resolving agents (as outlined in Scheme 6), as we believed these would mimic our original mutual kinetic resolution involving racemic oxazolidinone (*rac*)-**6** (in Scheme 5). Treatment of an equimolar amount of oxazoldinones (*R*)-**6** and (*S*)-**7** with *n*-butyl lithium, followed by the addition of a solution of racemic active ester (*rac*)-**17** and (*rac*)-**18** in THF at −78 °C, gave a pair of separable *quasi*-enantiomeric adducts *syn*-**19** and *syn*-**21**, and *syn*-**20** and *syn*-**22**, respectively, in good yield (Scheme 6). The levels of diastereocontrol were good (64–78% de), and most importantly were comparable to those shown for their corresponding mutual recognitions.

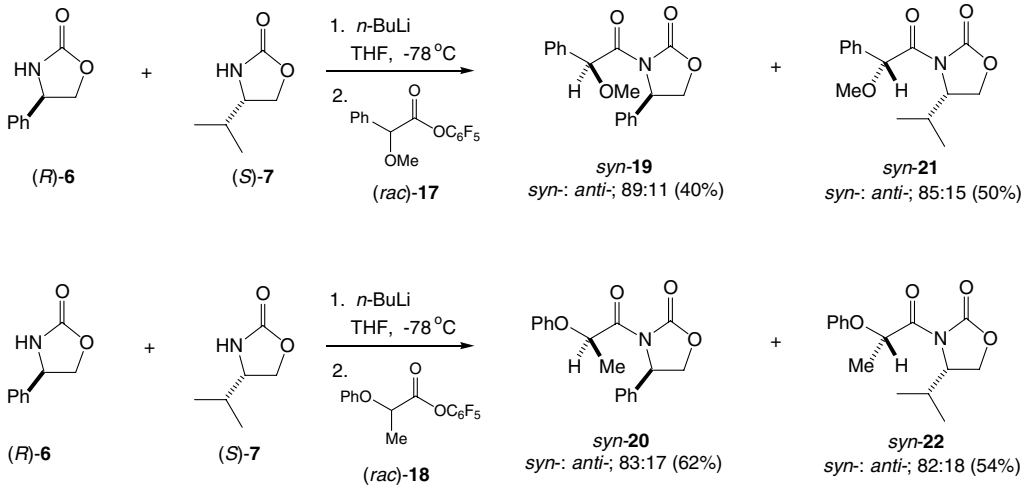
The required resolutions of 2-methoxy-2-phenyl acetic acid (*rac*)-**15** and 2-phenoxy-2-phenylpropionic acid (*rac*)-**16** were achieved through simple hydrolysis of adducts *syn*-**19**, *anti*-**19**, *syn*-**20** and *anti*-**20** using a combination of LiOH and H_2O_2 to give the corresponding 2-methoxy-2-phenyl acetic acids (*S*)-**15** and (*R*)-**15**, and 2-phenoxy-2-phenylpropionic acid (*S*)-**16** and (*R*)-**16** in good yield (Scheme 7). The absolute stereochemistry was assigned by comparison with the specific rotation of known literature values. The enantiomeric purity was determined by simple re-derivatisation by the formation of the corresponding pentafluorophenyl active esters, followed by sequential addition to the lithiated oxazolidinone derived from (*R*)-**6**.



Scheme 7. Hydrolysis of oxazolidinones *syn*-**19**, *anti*-**19**, *syn*-**20** and *anti*-**20**.

3. Conclusion

In conclusion, we report an efficient parallel kinetic resolution of pentafluorophenyl 2-methoxy-2-phenyl acetate (*rac*)-**17** and pentafluorophenyl 2-phenoxypropionate (*rac*)-**18** (derived from (*rac*)-**15** and (*rac*)-**16**, respectively)



Scheme 6. Parallel kinetic resolution of active esters (*rac*)-**17** and (*rac*)-**18** using a combination of oxazolidinones (*R*)-**6** and (*S*)-**7**.

using an equimolar amount of *quasi*-enantiomeric oxazolidinones (*R*)-**6** and (*S*)-**7**. This resolution methodology appears to be efficient for a range of substituted 2-hydroxy carboxylic acid derivatives, giving access to both enantiomerically pure forms of 2-methoxy-2-phenyl acetic acid **15** and 2-phenoxypropionic acid (*rac*)-**16** in good yield. The nearest analogy to this work is that reported by Fox[17] and Davies.[18] Fox[17] has shown the use of a combination of designer oxazolidinones to resolve racemic anhydrides, and has recently desymmetrised a series of *meso*-esters using methodology related to our parallel kinetic resolution.[19] By comparison, Davies[18] has kinetically resolved a series of 2-acetoxy acid chlorides using a SuperQuat[20] oxazolidinone to give adducts in high diastereoselectivity. We are currently examining the effect of competitive Lewis basicity on the mechanistic outcome of these mutual/parallel kinetic resolutions, and this study will be reported in due course.

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 250 MHz and 400 MHz Fourier transform spectrometers 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.

4.2. Synthesis of active esters

4.2.1. Pentafluorophenyl 2-methoxyphenylacetate (*rac*)-17. *N*,*N*′-Dicyclohexylcarbodiimide (1.37 g, 6.61 mmol) was slowly added to a stirred solution of 2-methoxy-phenylacetic acid (*rac*)-**15** (1.0 g, 6.01 mmol) in dichloromethane (10 ml) at room temperature. The resulting solution was stirred for 15 min. A solution of pentafluorophenol (1.11 g, 6.01 mmol) in dichloromethane (3 ml) was slowly added and the solution was stirred for a further 12 h. The resulting 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 hexane–diethyl ether (9:1) to give active ester (*rac*)-**17** (1.13 g, 57%) as a colourless oil; R_F [light petroleum bp (40–60 °C)–diethyl ether (8:2)] 0.66; υ_{max} (CH_2Cl_2); cm^{-1} 1793 (C=O) and 732 (CH; Ph); δ_H (270 MHz, $CDCl_3$) 7.53–7.49 (2H, m, 2 × CH; Ph), 7.44–7.40 (3H, m, 3 × CH; Ph), 5.10 (1H, s, CHO) and 3.51 (3H, s, CH_3); δ_C (100 MHz; $CDCl_3$) 167.0 (OC=O), 141.1 (142.19 and 139.68, 2C, ddt, $^1J_{C,F} = 250.6$ Hz, $^2J_{C,F} = 12.2$ Hz and $^3J_{C,F} = 3.8$ Hz, C(2)–F), 139.6 (140.83 and 138.31, 1C, dtt, $^1J_{C,F} = 252.1$ Hz, $^2J_{C,F} = 12.9$ Hz and $^3J_{C,F} = 3.9 = 8$ Hz, C(4)–F), 138.7 (*i*-C; Ph), 137.8 (139.03 and 136.52, 2 C, dtdd, $^1J_{C,F} = 249.8$ Hz, $^2J_{C,F} = 14.5$ Hz, $^3J_{C,F} = 5.7$ Hz and $^4J_{C,F} = 2.3$ Hz, C(3)–F), 134.5 (*i*-C; Ph), 129.4,[1] 128.8[2] and 127.2[2] (3 × CH; Ph), 82.0 (CHO) and 57.5 (OCH_3); δ_F (378 MHz; $CDCl_3$) −152.2 (2F, d, $^3J_{F,F}$ 20.9, F_{ortho}), −157.9 (1F, t, $^3J_{F,F}$ 20.9, F_{para}) and −161.9 (2F, t, $^3J_{F,F}$ 20.9, F_{meta}) (Found MNH_4^+ 350.0810. $C_{15}H_{13}F_5NO_3^+$ requires MNH_4^+ 350.0810).

4.2.2. Pentafluorophenyl 2-phenoxypropionate (*rac*)-18. In the same way as active ester (*rac*)-**17**, 2-phenoxypropionic acid (*rac*)-**16** (1.0 g, 6.02 mmol), DCC (1.25 g, 6.62 mmol) and pentafluorophenol (1.10 g, 6.02 mmol) gave active ester (*rac*)-**18** (1.28 g, 64%) as a colourless oil; R_F [light petroleum bp (40–60 °C)–diethyl ether (9:1)] 0.50; mp = 78–79 °C; υ_{max} ($CHCl_3$); cm^{-1} 1788 (C=O); δ_H (400 MHz; $CDCl_3$) 7.34–7.29 (2H, m, 2 × CH; OPh), 7.03 (1H, t, *J* 7.3, CH; OPh), 6.94 (2H, d, *J* 8.5, 2 × CH; OPh), 5.08 (1H, q, *J* 6.9, C*H*CH_3) and 1.82 (3H, d, *J* 6.9, CH_3CH); δ_C (100.6 MHz; $CDCl_3$) 168.5 (C=O), 157.1 (*i*-CO; Ph), 141.1 (142.36 and 139.85, 2C, ddt, $^1J_{C,F} = 251.3$ Hz, $^2J_{C,F} = 12.2$ Hz and $^3J_{C,F} = 3.8$ Hz, C(2)–F), 139.8 (141.03 and 138.50, 1C, dtt, $^1J_{C,F} = 252.2$ Hz, $^2J_{C,F} = 12.9$ Hz and $^3J_{C,F} = 3.8$ Hz, C(4)–F), 137.9 (139.17 and 136.65, 2C, dtdd, $^1J_{C,F} = 251.3$ Hz, $^2J_{C,F} = 14.5$ Hz, $^3J_{C,F} = 5.7$ Hz and $^4J_{C,F} = 2.2$ Hz, C(3)–F), 124.6 (1C, tt, $^2J_{C,F} = 12.2$ Hz and $^3J_{C,F} = 4.0$ Hz, *i*-C; C_6F_5), 129.7, 122.3 and 115.0 (3 × CH; OPh), 72.1 (PhCH) and 18.7 (CH_3); δ_F (378 MHz; $CDCl_3$) −152.5 (2F, d, $^3J_{F,F}$ 21.9, F_{ortho}), −156.9 (1F, t, $^3J_{F,F}$ 21.9, F_{para}) and −161.7 (2F, t, $^3J_{F,F}$ 21.9, F_{meta}) (Found M^+, 332.0470; $C_{15}H_9F_5O_3^+$ requires 332.0466).

4.3. Mutual kinetic resolutions

4.3.1. (4*RS*,2*SR*)-(2-Methoxy-2-phenylacetyl)-4-phenyl-oxazolidin-2-one *syn*-20 and (4*RS*,2*RS*)-(2-methoxy-2-phenylacetyl)-4-phenyl-oxazolidin-2-one *anti*-20. *n*-BuLi (0.52 ml, 2.5 M in hexanes, 1.28 mmol) was added to a stirred solution of oxazolidinone (*rac*)-**6** (0.20 g, 1.20 mmol) in THF at −78 °C. After stirring for 1 h, a solution of active ester (*rac*)-**17** (0.40 g, 1.28 mmol) in THF (5.0 ml) was added. The resulting mixture was stirred for 2 h at −78 °C. The reaction was quenched with water (10 ml). The organic layer was extracted with diethyl ether (2 × 10 ml), dried (over $MgSO_4$) and evaporated under reduced pressure to give a separable mixture of two diastereoisomers (ratio: *anti*:*syn* 86:14) of oxazolidinones *anti*- and *syn*-**19**. The residue was purified by flash column chromatography on silica gel eluting with light petroleum (bp 40–60 °C)–diethyl ether (7:3) to give oxazolidinone *syn*-**19** (0.15 g, 38%) as a colourless oil; R_F [light petroleum (bp 40–60 °C)–diethyl ether (1:1)] 0.14; υ_{max} (film); cm^{-1} 1782 (C=O) and 1715 (C=O); δ_H (400 MHz, $CDCl_3$) 7.36–7.12 (8 H, m, 8 × CH; Ph_A and Ph_B), 6.83 (2H, d, *J* 7.2, 2 × CH; Ph_A), 6.05 (1H, s, CHO), 5.47 (1H, dd, *J* 8.9 and 5.2, CHN), 4.67 (1H, t, *J* 8.9, CH_AH_BO), 4.10 (1H, dd, *J*

8.9 and 5.2, CH_AH_BO) and 3.35 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 170.4 (C=O), 153.6 (C=O), 138.0 (*i*-C; Ph_A), 135.3 (*i*-C; Ph_B), 129.6, 129.3, 129.2, 129.1, 128.9 and 126.1 (6 × C–H; Ph_A and Ph_B), 81.6 (CHO), 70.6 (CH_2O), 57.9 (NCH) and 57.6 (CH_3) (Found MNH_4^+ 329.1496. $C_{18}H_{21}N_2O_4^+$ requires MNH_4^+ 329.1496); and oxazolidinone *anti*-**19** (52 mg, 13%) as white needle-like crystals; R_F [light petroleum (40–60 °C)–diethyl ether (1:1)] 0.37; mp 104–106 °C; υ_{max} (CH_2Cl_2)/cm^{-1} 1782 (C=O) and 1718 (C=O); δ_H (270 MHz, $CDCl_3$) 7.53–7.49 (2H, m, 2 × CH; Ph_A), 7.36–7.31 (8H, m, 8 × CH; Ph_A and Ph_B), 6.00 (1H, s, CHCO), 5.32 (1H, dd, *J* 8.6 and 3.2, CHN), 4.56 (1H, t, *J* 8.6, CH_AH_BO), 4.26 (1H, dd, *J* 8.6 and 3.2, CH_AH_BO) and 3.25 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 170.1 (C=O), 153.0 (C=O), 138.8 (*i*-C; Ph_A), 135.4 (*i*-C; Ph_B), 129.2[1], 129.0[1], 128.8[2], 128.6[1] and 125.9[1] (6 × C–H; Ph_A and Ph_B), 80.6 (CHCO), 70.3 (CH_2O), 58.0 (NCH) and 57.0 (CH_3) (Found M^+ 311.1152. $C_{18}H_{17}NO_4^+$ requires M^+ 311.1152).

4.3.2. (4*RS*,2*RS*)-(2-Phenoxypropionyl)-4-phenyl-oxazolidin-2-one *syn*-20 and (4*RS*,2*SR*)-(2-phenoxypropionyl)-4-phenyl-oxazolidin-2-one *anti*-20. In the same way as the above, *n*-butyl lithium (0.52 ml, 2.5 M in hexane, 1.28 mmol), oxazolidinone (*rac*)-**6** (0.20 g, 1.22 mmol) and active ester (*rac*)-**18** (0.40 g, 1.28 mmol), gave a crude mixture of oxazolidinones *syn*-**20** and *anti*-**20** (ratio 89:11). The residue was purified by flash column chromatography on silica gel eluting with light petroleum (bp 40–60 °C)–diethyl ether (7:3) to give oxazolidinone *syn*-**20** (0.21 g, 52%) as a white solid; mp = 73–76 °C; R_F [light petroleum (40–60 °C)–diethyl ether (1:1)] 0.20; υ_{max}/cm^{-1} ($CHCl_2$) 1782 (C=O) and 1715 (C=O); δ_H (270 MHz, $CDCl_3$) 7.34–7.24 (5H, m, 5 × CH, Ph), 7.11 (2H, t, *J* 7.7, 2 × CH; Ph), 6.86 (1H, t, *J* 7.4, 1 × CH; Ph), 5.88 (1H, q, *J* 6.4, C*H*CH_3), 5.44 (1H, dd, *J* 8.9 and 3.5, CHN), 4.76 (1H, t, *J* 8.9, CH_AH_BO), 4.36 (1H, dd, *J* 8.9 and 3.5, CH_AH_BO), 1.63 (3H, d, *J* 6.4, CHCH_3); δ_C (100 MHz, $CDCl_3$) 171.6 (C=O), 157.1 (C=O), 153.5 (*i*-CO; OPh), 136.4 (*i*-C; Ph), 129.4, 129.2, 128.9, 126.0, 121.5 and 115.3 (6 × CH; Ph and OPh), 71.9 (CH_2O), 70.7 ($CHCH_3$), 57.8 (CHN) and 18.2 (CH_3) (Found MH^+, 312.1244; $C_{18}H_{18}NO_4$ requires MH^+, 312.1236); and the oxazolidinone *anti*-**20** (39 mg, 10%) as an oil; R_F [light petroleum (bp 40–60 °C)–ether (1:1)] 0.39; υ_{max}/cm^{-1} ($CHCl_2$) 1780 (C=O) and 1718 (C=O); δ_H (270 MHz, $CDCl_3$) 7.37–7.21 (7H, m, 7 × CH; 2 × Ph), 6.94 (1H, t, *J* 7.8, 1 × CH; Ph), 6.86 (2H, d, *J* 7.9, 2 × CH; Ph), 5.99 (1H, q, *J* 6.7, C*H*CH_3), 5.44 (1H, dd, *J* 8.9 and 4.5, CHN), 4.76 (1H, t, *J* 8.9, CH_ACH_BO), 4.35 (1H, dd, *J* 8.9 and 4.5; CH_ACH_BO) and 1.54 (3H, d, *J* 6.7, CHCH_3); δ_C (100 MHz, $CDCl_3$) 171.4 (C=O), 157.2 (C=O), 153.3 (*i*-CO; OPh), 138.2 (*i*-C; Ph), 129.5, 129.2, 128.9, 126.0, 121.6 and 115.2 (6 × CH; Ph and OPh), 71.5 (CH_2O), 70.6 (CHMe), 57.5 (CHN) and 18.0 (CH_3) (Found MH^+ 312.1244; $C_{18}H_{18}NO_4$ requires MH^+, 312.1236).

4.3.3. Parallel kinetic resolution of active ester (*rac*)-17 using oxazolidinones (*R*)-6 and (*S*)-7. In the same way as the above, *n*-butyl lithium (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone (*R*)-**6** (0.105 g, 0.64 mmol), oxazolidinone (*S*)-**7** (83 mg, 0.64 mmol) and active ester (*rac*)-**17** (0.50 g, 1.55 mmol), gave a crude mixture of oxazolidinones*syn*-**19** and *anti*-**19** (ratio 89:11) and *syn*-**21** and *anti*-**21** (ratio 85:15). The residue was purified by flash column chromatography on silica gel eluting with light petroleum (bp 40–60 °C)–diethyl ether (7:3) to give oxazolidinone *syn*-**19** (65 mg, 33%) as white needle-like crystals; R_F [light petroleum (40–60 °C)–diethyl ether (1:1)] 0.37; mp 92–98 °C; $[\alpha]_D^{23} = -14.4$ (*c* 0.22, $CHCl_3$); υ_{max} (CH_2Cl_2)/cm^{-1} 1782 (C=O) and 1718 (C=O); δ_H (270 MHz, $CDCl_3$) 7.36–7.12 (8H, m, 8 × CH; Ph_A and Ph_B), 6.83 (2H, d, *J* 7.2, 2 × CH; Ph_A), 6.05 (1H, s, CHO), 5.47 (1H, dd, *J* 8.9 and 5.2, CHN), 4.67 (1H, t, *J* 8.9, CH_AH_BO), 4.10 (1H, dd, *J* 8.9 and 5.2, CH_AH_BO) and 3.35 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 170.4 (C=O), 153.6 (C=O), 138.0 (*i*-C; Ph_A), 135.3 (*i*-C; Ph_B), 129.6, 129.3, 129.2, 129.1, 128.9 and 126.1 (6 × C–H; Ph_A and Ph_B), 81.6 (CHO), 70.6 (CH_2O), 57.9 (NCH) and 57.6 (CH_3) (Found MNH_4^+ 329.1496. $C_{18}H_{21}N_2O_4^+$ requires MNH_4^+ 329.1496); *anti*-**19** (13 mg, 7%); R_F [light petroleum (40–60 °C)–diethyl ether (1:1)] 0.37; mp 164–165 °C; $[\alpha]_D^{23}$ − 194.7 (*c* 0.72, $CHCl_3$); υ_{max} (CH_2Cl_2)/cm^{-1} 1782 (C=O) and 1718 (C=O); δ_H (270 MHz, $CDCl_3$) 7.53–7.49 (2H, m, 2 × CH; Ph_A), 7.36–7.31 (8H, m, 8 × CH; Ph_A and Ph_B), 6.00 (1H, s, CHCO), 5.32 (1H, dd, *J* 8.6 and 3.2, CHN), 4.56 (1H, t, *J* 8.6, CH_AH_BO), 4.26 (1H, dd, *J* 8.6 and 3.2, CH_AH_BO) and 3.25 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 170.1 (C=O), 153.0 (C=O), 138.8 (*i*-C; Ph_A), 135.4 (*i*-C; Ph_B), 129.2[1], 129.0[1], 128.8[2], 128.6[1] and 125.9[1] (6 × C–H; Ph_A and Ph_B), 80.6 (CHCO), 70.3 (CH_2O), 58.0 (NCH) and 57.0 (CH_3) (Found M^+ 311.1152. $C_{18}H_{17}NO_4^+$ requires M^+ 311.1152); *syn*-**21** (76 mg, 43%) as an oil; R_F [light petroleum (40–60 °C)–diethyl ether (1:1)] 0.19; $[\alpha]_D^{23} = -10.8$ (*c* 2.71, $CHCl_3$); υ_{max} (CH_2Cl_2)/cm^{-1} 1782 (C=O) and 1717 (C=O); δ_H (270 MHz, $CDCl_3$) 7.51–7.47 (2H, m, 2 × CH; Ph), 7.33–7.28 (3H, m, 3 × CH; Ph), 6.06 (1H, s, CHO), 4.53–4.47 (1H, m, CHN), 4.27 (1H, t, *J* 9.1, CH_AH_BO), 4.09 (1H, dd, *J* 9.1 and 3.7, CH_AH_BO), 3.34 (3H, s, OCH_3), 2.14–2.03 (1H, m, C*H*$(CH_3)_2$), 0.72 (3H, d, *J* 6.9, CH_3) and 0.34 (3H, d, *J* 6.9, CH_3); δ_C (100 MHz, $CDCl_3$) 171.1 (C=O), 153.9 (C=O), 136.0 (*i*-C; Ph), 129.3, 128.9 and 128.9, (3 × CH; Ph), 81.1 (CHO), 64.0 (CH_2O), 58.3 (NCH), 57.5 (CH_3O), 29.4 (*C*H$(CH_3)_2$), 17.9 (CH_3) and 15.6 (CH_3) (Found MNH_4^+ 295.1654. $C_{15}H_{23}N_2O_4$ requires MNH_4^+ 295.1652); *anti*-**21** (12 mg, 7%) as an oil; R_F [light petroleum (40–60 °C)–diethyl ether (7:3)] 0.51; $[\alpha]_D^{23} = +138.0$ (*c* 0.28, $CHCl_3$); υ_{max} (CH_2Cl_2)/cm^{-1} 1782 (C=O) and 1717 (C=O); δ_H (270 MHz, $CDCl_3$) 7.51–7.47 (2H, m, 2 × CH; Ph), 7.36–7.32 (3H, m, 3 × CH; Ph), 6.04 (1H, s, CHO), 4.36–4.29 (1H, m, CHN), 4.20–4.09 (2H, m, CH_2O), 3.35 (3H, s, CH_3), 2.57–2.45 (1H, m, C*H*$(CH_3)_2$), 0.92 (3H, d, *J* 6.9, $CH_3^ACHCH_3^B$) and 0.91 (3H, d, *J* 6.9, $CH_3^ACHCH_3^B$); δ_C (100 MHz, $CDCl_3$) 171.0 (C=O), 153.9 (C=O), 135.8 (*i*-C; Ph), 129.4, 129.1 and 129.0 (3 × CH; Ph), 80.9 (CHCO), 64.0 (CH_2O), 59.5 (NCH), 57.4 (CH_3O), 28.7 (*C*H$(CH_3)_2$), 18.3 (CH_3) and 15.6 (CH_3) (Found MNH_4^+ 295.1657. $C_{15}H_{23}N_2O_4$ requires MNH_4^+ 295.1652).

4.3.4. Parallel kinetic resolution of active ester (*rac*)-18 using oxazolidinones (*R*)-6 and (*S*)-7. In the same way as the above, *n*-butyl lithium (0.54 ml, 2.5 M in hexane, 1.34 mmol), oxazolidinone (*R*)-**6** (98 mg, 0.61 mmol),

oxazolidinone (*S*)-**7** (78 mg, 0.61 mmol) and active ester (*rac*)-**18** (0.40 g, 1.23 mmol), gave a crude mixture of oxazolidinones *syn*-**20** and *anti*-**20** (ratio 83:17) and *syn*-**22** and *anti*-**22** (ratio 85:15). The residue was purified by flash column chromatography on silica gel eluting with light petroleum (bp 40–60 °C)–diethyl ether (7:3) to give oxazolidinone *syn*-**20** (91 mg, 48%) as white needle-like crystals; R_F [light petroleum (bp 40–60 °C)–ether (1:1)] 0.20; mp 121–123 °C; $[\alpha]_D^{23} = +24.2$ (*c* 0.45, $CHCl_3$); υ_{max}/cm^{-1} ($CHCl_2$) 1782 (C=O) and 1715 (C=O); δ_H (270 MHz, $CDCl_3$) 7.34–7.24 (5H, m, 5 × CH, Ph), 7.11 (2H, t, *J* 7.7, 2 × CH; Ph), 6.86 (1H, t, *J* 7.4, 1 × CH; Ph), 5.88 (1H, q, *J* 6.4, C*H*CH_3), 5.44 (1H, dd, *J* 8.9 and 3.5, CHN), 4.76 (1H, t, *J* 8.9, CH_AH_BO), 4.36 (1H, dd, *J* 8.9 and 3.5, CH_AH_BO) and 1.63 (3H, d, *J* 6.4, CHCH_3); δ_C (100 MHz, $CDCl_3$) 171.6 (C=O), 157.1 (C=O), 153.5 (*i*-CO; OPh), 136.4 (*i*-C; Ph), 129.4, 129.2, 128.9, 126.0, 121.5 and 115.3 (6 × CH; Ph and OPh), 71.9 (CH_2O), 70.7 ($CHCH_3$), 57.8 (CHN) and 18.2 (CH_3) (Found MNH_4^+, 312.1244; $C_{18}H_{21}N_2O_4$ requires MNH_4^+, 312.1236); oxazolidinone *anti*-**20** (27 mg, 14%) as a white solid; R_F [light petroleum (bp 40–60 °C)–ether (1:1)] 0.39; mp 151–153 °C; $[\alpha]_D^{23} = -171.1$ (*c* 0.54, $CHCl_3$); υ_{max}/cm^{-1} ($CHCl_2$) 1780 (C=O) and 1718 (C=O); δ_H (270 MHz, $CDCl_3$) 7.37–7.21 (7H, m, 7 × CH; 2 × Ph), 6.94 (1H, t, *J* 7.8, 1 × CH; Ph), 6.86 (2H, d, *J* 7.9, 2 × CH; Ph), 5.99 (1H, q, *J* 6.7, C*H*CH_3), 5.44 (1H, dd, *J* 8.9 and 4.5, CHN), 4.76 (1H, t, *J* 8.9, CH_ACH_BO), 4.35 (1H, dd, *J* 8.9 and 4.5; CH_ACH_BO), 1.54 (3H, d, *J* 6.7, CHCH_3); δ_C (100 MHz, $CDCl_3$) 171.4 (C=O), 157.2 (C=O), 153.3 (*i*-CO; OPh), 138.2 (*i*-C; Ph), 129.5, 129.2, 128.9, 126.0, 121.6 and 115.2 (6 × CH; Ph and OPh), 71.5 (CH_2O), 70.6 (CHMe), 57.5 (CHN) and 18.0 (CH_3) (Found MNH_4^+ 312.1244; $C_{18}H_{21}N_2O_4$ requires MNH_4^+, 312.1236); *syn*-**22** (74 mg, 44%) as a white solid; R_F [light petroleum (bp 40–60 °C)–ether (1:1)] 0.36; mp 72–74 °C; $[\alpha]_D^{23} = +13.4$ (*c* 2.2, $CHCl_3$); υ_{max}/cm^{-1} ($CHCl_2$) 1780 (C=O) and 1714 (C=O); δ_H (400 MHz, $CDCl_3$) 7.20–7.15 (2H, m, 2 × CH, Ph), 6.90–6.85 (1H, t, *J* 7.3, 1 × CH; Ph), 6.82–6.79 (2H, m, 2 × CH; Ph), 5.94 (1H, q, *J* 6.6, C*H*CH_3), 4.39–4.35 (1H, m, CHN), 4.27 (1H, t, *J* 9.1, CH_AH_BO), 4.20 (1H, dd, *J* 9.1 and 3.0, CH_AH_BO), 2.31–2.23 (1H, m, C*H*$(CH_3)_2$), 1.54 (3H, d, *J* 6.6, CHCH_3), 0.80 (3H, d, *J* 6.9, $CH_3^ACHCH_3^B$) and 0.80 (3H, d, *J* 6.9, $CH_3^ACHCH_3^B$); δ_C (100 MHz, $CDCl_3$) 172.1 (C=O), 157.1 (C=O), 153.7 (*i*-CO; OPh), 129.5, 121.4 and 114.9 (3 × CH; Ph), 71.2 (CH_2O), 63.8 ($CHCH_3$), 58.6 (CHN), 27.9 ($CH(CH_3)_2$), 18.1 (CH_3), 17.8 (CH_3) and 14.3 (CH_3) (Found MH^+ 278.1400; $C_{15}H_{19}NO_4$ requires 278.1392); *anti*-**22** (17 mg, 10%) as a white solid; R_F [light petroleum (bp 40–60 °C)–ether (1:1)] 0.39; mp 75–78 °C; $[\alpha]_D^{23} = +79.5$ (*c* 2.3, $CHCl_3$); υ_{max}/cm^{-1} ($CHCl_2$) 1780 (C=O) and 1718 (C=O); δ_H (270 MHz, $CDCl_3$) 7.25 (2H, t, *J* 7.4, 2 × CH, Ph), 6.94 (1H, t, *J* 7.4, 1 × CH; Ph), 6.86 (2H, d, *J* 7.4, 2 × CH; Ph), 5.97 (1H, q, *J* 6.7, CHO), 4.51–4.45 (1H, m, CHN), 4.35 (1H, t, *J* 9.1, CH_AH_BO), 4.25 (1H, dd, *J* 9.1 and 3.5, CH_AH_BO), 2.40–2.26 (1H, m, C*H*$(CH_3)_2$), 1.67 (3H, d, *J* 6.7, CHCH_3), 0.89 (3H, d, *J* 6.9, $(CH_3)_ACH(CH_3)_B$) and 0.88 (3H, d, *J* 6.9, $(CH_3)_A$ $CH(CH_3)_B$); δ_C (100 MHz, $CDCl_3$) 172.1 (C=O), 157.3 (C=O), 153.7 (*i*-CO; Ph), 129.5, 121.6, 115.2 (3 × CH; Ph), 71.7 (CH_2O), 64.3 ($CHCH_3$), 58.2 (CHN), 28.3 ($CHMe_2$), 18.7 (CH_3), 17.7 (CH_3) and 14.8 (CH_3) (Found MH^+ 278.1400; $C_{15}H_{19}NO_4^+$ requires 278.1392).

4.3.5. Hydrolysis of oxazolidinone adducts *anti*- and *syn*-19 (+)-2-methoxy-2-phenylacetic acid (*S*)-15. Lithium hydroxide monohydrate (34 mg, 0.82 mmol) was slowly added to a stirred solution of oxazolidinone *syn*-**21** (127 mg, 0.41 mmol) and hydrogen peroxide (27 mg, 0.82 mmol, 30% v/w) 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 to give the recovered oxazolidinone (*R*)-**6** (55 mg, 83%) as a white solid. The aqueous phase was acidified using HCl (3 M HCl) until the pH = 3, and extracted with diethyl ether (3 × 10 ml). The combined organic phases were dried (over $MgSO_4$) and evaporated under reduced pressure to give (*S*)-2-methoxy-2-phenylacetic acid (*S*)-**15** (65 mg, 96%) as an oil; R_F [diethyl ether] 0.54; $[\alpha]_D^{23} = 141.0$ (*c* 4.7, $CHCl_3$), {lit.[21] for (*R*)-; $[\alpha]_D = -141.8$ (*c* 0.13, $CHCl_3$)}; $\nu_{max}(CHCl_3)$; cm^{-1} 1725 (C=O); δ_H (400 MHz; $CDCl_3$) 8.60 (1H, br s, OH), 7.37–7.35 (2H, m, 2 × CH; Ph), 7.30–7.25 (3H, m, 3 × CH; Ph), 4.70 (1H, s, CH) and 3.33 (3H, s, OCH_3); δ_C (100 MHz; $CDCl_3$) 175.3 (C=O), 135.3 (*i*-C; Ph), 129.0, 128.7 and 127.2 (3 × CH; Ph), 81.9 (CH) and 57.2 (OCH_3) (Found M^+ 166.0622. $C_9H_{10}O_3^+$ requires 166.0624).

4.3.6. (−)-2-Methoxy-2-phenylacetic acid (*R*)-15. In the same way as for oxazolidinone *syn*-**19**, oxazolidinone *anti*-**19** (218 mg, 0.70 mmol), lithium hydroxide monohydrate (59 mg, 1.40 mmol) and hydrogen peroxide (48 mg, 1.40 mmol, 30% v/w), gave after extraction the recovered oxazolidinone (*R*)-**6** (94 mg, 82%) as a white solid; and (*R*)-2-methoxy-2-phenylacetic acid (*R*)-**15** (110 mg, 95%) as an oil; R_F [diethyl ether] 0.54; $[\alpha]_D^{23} = -140.2$ (*c* 4.4, $CHCl_3$), {lit.[21] $[\alpha]_D = -141.8$ (*c* 0.13, $CHCl_3$)}; $\nu_{max}(CHCl_3)$; cm^{-1} 1724 (C=O); δ_H (400 MHz; $CDCl_3$) 9.29 (1H, br s, OH), 7.37–7.35 (2H, m, 2 × CH; Ph), 7.32–7.26 (3H, m, 3 × CH; Ph), 4.70 (1H, s, CH) and 3.32 (3H, s, OCH_3); δ_C (100 MHz; $CDCl_3$) 175.6 (C=O), 135.3 (*i*-C; Ph), 128.9, 128.7 and 127.2 (3 × CH; Ph), 81.9 (CH) and 57.2 (OCH_3) (Found MNH_4^+ 184.0968. $C_9H_{14}NO_3^+$ requires 184.0968).

4.3.7. (−)-2-Phenoxypropionic acid (*S*)-16. In the same way as oxazolidinone *syn*-**19**, oxazolidinone *syn*-**20** (0.701 g, 2.25 mmol), lithium hydroxide monohydrate (0.319 g, 4.50 mmol) and hydrogen peroxide (0.15 g, 4.50 mmol), gave after extraction the recovered oxazolidinone (*R*)-**6** (0.33 g, 90%) as a white solid and 2-phenoxypropionic acid (*S*)-**16** (0.34 g, 91%) as a white solid; R_F [diethyl ether] 0.89; mp 82–84 °C; $[\alpha]_D^{23} = -23.4$ (*c* 3.7, $CHCl_3$); υ_{max}/cm^{-1} (CH_2Cl_2) 1728 (C=O); δ_H (270 MHz, $CDCl_3$); 7.32–7.24 (2H, m, 3 × CH; Ph), 6.99 (1H, t, *J* 7.1, CH; Ph), 6.89 (2H, d, *J* 8.6, 2 × CH; Ph), 4.79 (1H, q, *J* 6.7, CHO) and 1.65 (3H, d, *J* 6.7, Me); δ_C (100 MHz, $CDCl_3$) 177.4 (C=O), 157.1 (*i*-CO; Ph), 129.7, 122.0 and 115.1 (3 × CH; Ph), 72.0 (PhOCH) and 18.4 (CH_3) (Found MNH_4^+ 184.0965. $C_9H_{14}NO_3^+$ requires 184.0968).

4.3.8. (+)-2-Phenoxypropionic acid (*R*)-16. In the same way as for oxazolidinone *syn*-**19**, oxazolidinone *anti*-**20** (0.72 g, 2.31 mmol), lithium hydroxide monohydrate (0.19 g, 4.63 mmol) and hydrogen peroxide (0.157 g, 0.14 ml, 4.63 mmol), gave after extraction the recovered oxazolidinone (*R*)-**6** (0.35 g, 93%) as a white solid and 2-phenoxypropionic acid (*R*)-**16** (0.32 g, 85%) as a white solid; R_F [diethyl ether] 0.89; mp 84–86 °C; $[\alpha]_D^{23} = +23.6$ (*c* 3.6, $CHCl_3$); υ_{max}/cm^{-1} (CH_2Cl_2) 1729 (C=O); δ_H (270 MHz, $CDCl_3$) 7.31–7.25 (2H, m, 3 × CH; Ph), 6.99 (1H, t, *J* 7.1, 1 × CH; Ph), 6.89 (2H, d, *J* 8.6, 2 × CH; Ph), 4.79 (1H, q, *J* 6.7, CHO) and 1.65 (3H, d, *J* 6.7, CH_3); δ_C (100 MHz, $CDCl_3$) 177.5 (C=O), 157.0 (*i*-CO; OPh), 129.7, 122.0 and 115.2 (3 × CH; Ph), 72.1 (CH) and 18.3 (CH_3) (Found MNH_4^+, 184.0967. $C_9H_{18}N_2O_3$ requires MNH_4^+, 184.0968).

Acknowledgements

We are grateful to Queen Mary, University of London for their financial support (to S.C.), The Royal Society and The University of London Central Research Fund for their financial support (to J.E.), the EPSRC National Mass Spectrometry Service (Swansea) for accurate mass determinations, and Marco Dingjan for his technical assistance.

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. Cat.* **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. (a) Davies, F. A.; Reddy, R. E.; Portonovo, P. S. *Tetrahedron Lett.* **1994**, *35*, 9351–9354; (b) Oppolzer, W.; Tamura, O. *Tetrahedron Lett.* **1990**, *31*, 991–994; (c) Badorrey, R.; Cativiela, C.; Diaz-de-Villegas, M. D.; Galvez, J. A. *Tetrahedron* **1997**, *53*, 1411–1416; (d) Ghosez, L.; Gouverneur, V. *Tetrahedron* **1996**, *52*, 7585–7598; Chakraborty, T. K.; Hussain, K. A.; Reddy, G. V. *Tetrahedron* **1995**, *51*, 9179–9190; (e) Youshko, M. I.; van Langen, L. M.; Sheldon, R. A.; Svedas, V. K. *Tetrahedron: Asymmetry* **2004**, *15*, 1933–1936; (f) Keil, O.; Schneider, M. P.; Rasor, J. P. *Tetrahedron: Asymmetry* **1995**, *6*, 1257–1260; (g) Caron, M.; Carlier, P. R.; Sharpless, K. B. *J. Org. Chem.* **1988**, *53*, 5185–5187; (h) Williams, R. M.; Hendrix, J. A. *J. Org. Chem.* **1990**, *55*, 3723–3728; (i) Scrimin, P.; Tecilla, P.; Tonellato, U. *J. Org. Chem.* **1994**, *59*, 4194–4201.
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. Nerurkar, S. G.; Dighe, S. V.; Williams, R. L. *J. Clin. Pharmacol.* **1992**, *32*, 935–943.
7. (a) Eames, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 885–890; (b) Eames, J. In *Parallel Kinetic Resolutions*. In *Organic Synthesis Highlights*; VCH-Wiley: Weinheim, 2003; Vol. V, Chapter 17, pp 151–164 (ISBN 3-527-30611-0); (c) Dehli, J. R.; Gotor, V. *Chem. Soc. Rev.* **2002**, *31*, 365–370.
8. Reported in Asymmetric Synthesis via Iron Acyl Complexes; Preston S. C.; D.Phil. Dissertation, Oxford University, 1989; *Diss. Abstr. Int. B,* **1990**, *51*, 2896.
9. Vedejs, E.; Chen, X. *J. Am. Chem. Soc.* **1997**, *119*, 2584–2585; For related examples, see: (a) Vedejs, E.; Rozners, E. *J. Am. Chem. Soc.* **2001**, *123*, 2428–2429; (b) Vedejs, E.; Daugulis, O. *J. Am. Chem. Soc.* **2003**, *125*, 4166–4173.
10. Davies, S. G.; Diez, D.; El Hammouni, M. M.; Garner, A. C.; Garrido, N. M.; Long, M. J.; Morrison, R. M.; Smith, A. D.; Sweet, M. J.; Withey, J. M. *Chem. Commum.* **2003**, 2410–2411; For related examples, see: (a) Davies, S. G.; Garner, A. C.; Long, M. J.; Smith, A. D.; Sweet, M. J.; Withey, J. M. *Org. Biomol. Chem.* **2004**, *2*, 3355–3362; (b) Davies, S. G.; Garner, A. C.; Long, M. J.; Morrison, R. M.; Roberts, P. M.; Savory, E. D.; Smith, A. D.; Sweet, M. J.; Withey, J. M. *Org. Biomol. Chem.* **2005**, *3*, 2762–2775.
11. Coumbarides, G. S.; Dingjan, M.; Eames, J.; Flinn, A.; Northen, J.; Yohannes, Y. *Tetrahedron Lett.* **2005**, *46*, 2897–2902.
12. Coumbarides, G. S.; Dingjan, M.; Eames, J.; Flinn, A.; Motevalli, M.; Northen, J.; Yohannes, Y. *Synlett* **2006**, 101–105.
13. Assignment of stereochemistry was confirmed through stereospecific synthesis.
14. A reversal of diastereoselectivity has been shown to occur for structurally related acid chlorides and pentafluorophenyl esters. For additional information and examples, see Refs. 15,16,18.
15. (a) Coumbarides, G. S.; Eames, J.; Flinn, A.; Northen, J.; Yohannes, Y. *Tetrahedron Lett.* **2005**, *46*, 849–853; (b) Chavda, S.; Coulbeck, E.; Coumbarides, G. S.; Dingjan, M.; Eames, J.; Ghilagaber, S.; Yohannes, Y. *Tetrahedron: Asymmetry* **2006**, *17*, 3386–3399.
16. Yohannes, Y. Ph.D. Thesis, University of London, 2004.
17. Liao, L.; Zhang, F.; Dmitrenko, O.; Bach, R. D.; Fox, J. M. *J. Am. Chem. Soc.* **2004**, *126*, 4490–4491.
18. Bew, S. P.; Davies, S. G.; Fukuzawa, S.-I. *Chirality* **2000**, *12*, 483–487.
19. Zhang, F.; Fox, J. M. *Org. Lett.* **2006**, *8*, 2965–2968.
20. Bull, S. D.; Davies, S. G.; Garner, A. C.; Kruchinin, D.; Key, M. S.; Roberts, P. M.; Savory, A. D.; Smith, A. D.; Thomson, J. E. *Org. Biomol. Chem.* **2006**, *4*, 2945–2964.
21. Prasad, K. R.; Chandrakumar, A. *Tetrahedron: Asymmetry* **2005**, *16*, 1897–1900.