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Investigations into the parallel kinetic resolution of 2-phenylpropanoyl chloride using quasi-enantiomeric oxazolidinones

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Abstract—The resolution of 2-phenylpropanoyl chloride using an equimolar combination of quasi-enantiomeric oxazolidinones is discussed. The levels of diastereoselectivity were found to be dependent upon the structural nature of the metallated oxazolidinone, temperature and metal counter-ion.
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1. Introduction

The synthesis of enantiomerically pure profens,[1] such as ibuprofen[2] and naproxen,[3] is well documented. In particular, the (*S*)-enantiomeric form has become pharmaceutically important due to its non-steroidal anti-inflammatory properties.[4] Over the last decade, a notable amount of attention has been focused on the design of novel methods[5] for their efficient industrial construction. More recently, the use of chiral auxiliaries,[6] such as Evans' original oxazolidinones[7] has attracted some attention. These approaches have focussed on the use of diastereoselective alkylation of chiral enolates[8] and simple derivatizations of substituted oxazolidinones. Of these two approaches, diastereoselective alkylation has been shown to give excellent levels of stereocontrol with considerable predictability.[9] By comparison, derivatization of enantiomerically pure lithiated oxazolidinones by the addition of racemic acid chlorides, even though synthetically shorter, is much less documented due to poor diastereocontrol.[10] For example, Fukuzawa[11]and Bettoni[12] have shown the resolution of 2-phenylpropanoyl chloride *rac*-**1** and (4-chlorophenoxy)propanoyl chloride *rac*-**2**, respectively, using a lithiated Evans oxazolidinone [derived from the deprotonation of (*S*)-**4** with *n*-butyl lithium], gave the corresponding adducts **5** and **6** with no levels of diastereocontrol (Scheme 1).

Whereas Davies[13] has shown the use of activated acid chlorides, such as *O*-acetyl mandelic chloride *rac*-**3** can give the corresponding adduct *anti*-**7** with moderate to good levels of diastereoselectivity (Scheme 1).

Davies has also investigated this poor stereodiscrimination,[13] and has discovered that SuperQuat oxazolidinones,[14] such as (*S*)-**8**, are capable of kinetically resolving *O*-acetyl mandelic chloride *rac*-**3** and related 2-acetoxy-2-cyclohexylacetyl chloride *rac*-**10** with good to high levels of diastereoselectivity, to give the corresponding *anti*-adducts **9** and **11** in high yields (95% and 88%, respectively) with excellent levels of diastereoisomeric control (Scheme 2). By contrast, Fukuzawa[11] has used an alternative coupling strategy[15] to improve the levels of diastereocontrol by the use of a copper (II) chloride mediated coupling of N-silylated oxazolidinone (*S*)-**12** and 2-phenylpropanoyl chloride *rac*-**1** (Scheme 2). This proved moderately successful, leading to the complementary *syn*-adduct **5** in a 49% yield as the major diastereoisomer (Scheme 2).

2. Results and discussion

Over the last few years, we have become interested[16] in the synthesis of enantiomerically pure profen adducts.[17] In particular, we have also probed[17a] the resolution of 2-phenylpropionic acid **10** by the addition of the lithiated oxazolidinone [derived from *n*-butyl lithium and (*S*)-**4**] to a solution of 2-phenylpropanoyl chloride *rac*-**3** (2 equiv) in

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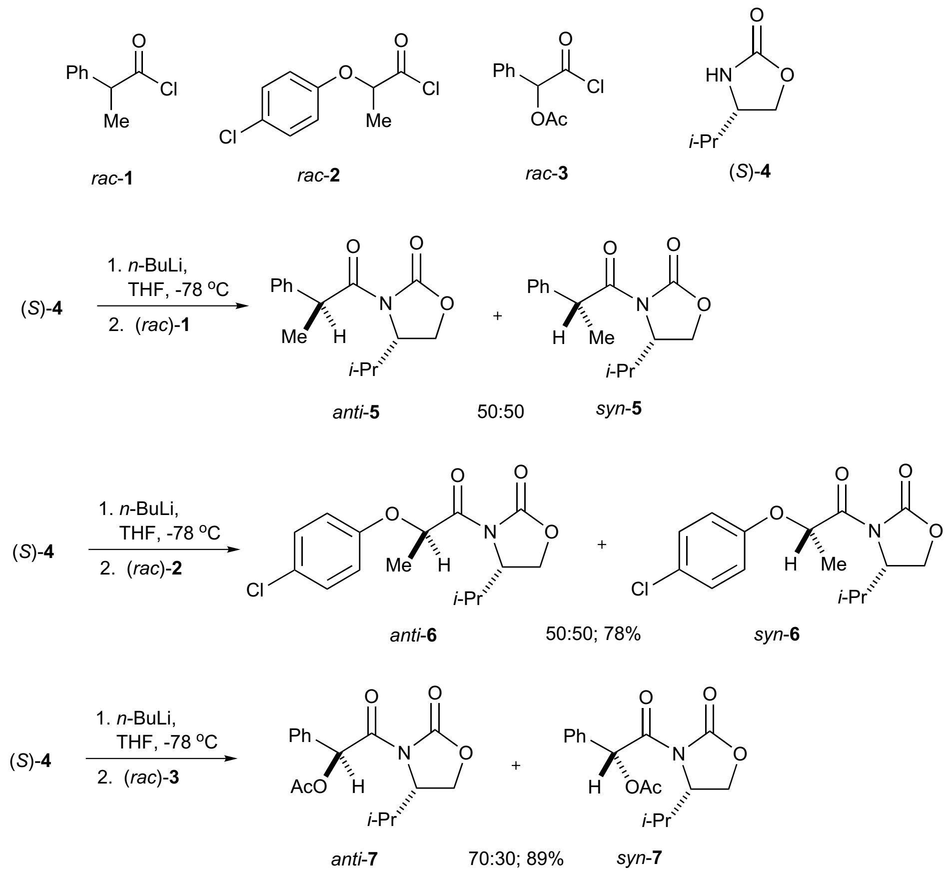
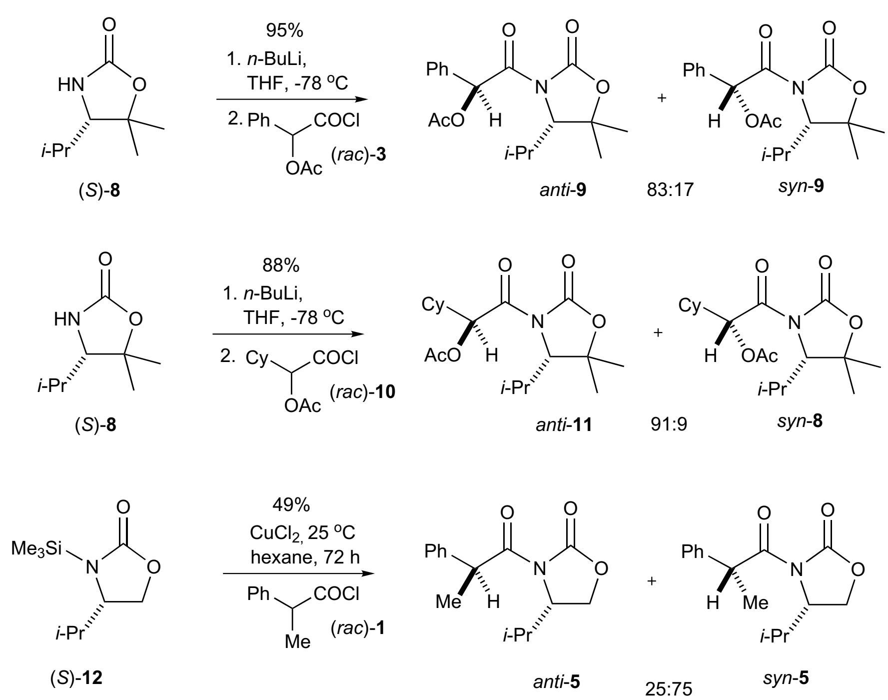


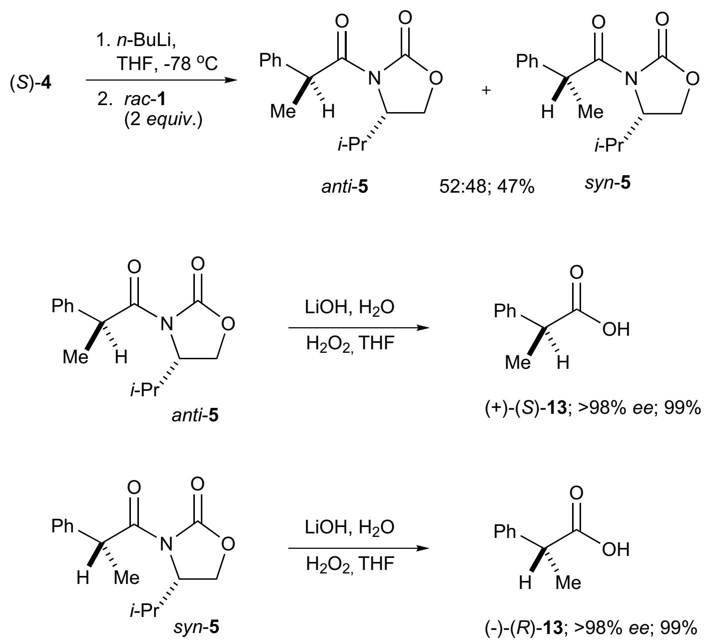
Scheme 1. Kinetic resolution of acid chlorides **1**, **2** and **3** using (*S*)-**4**.



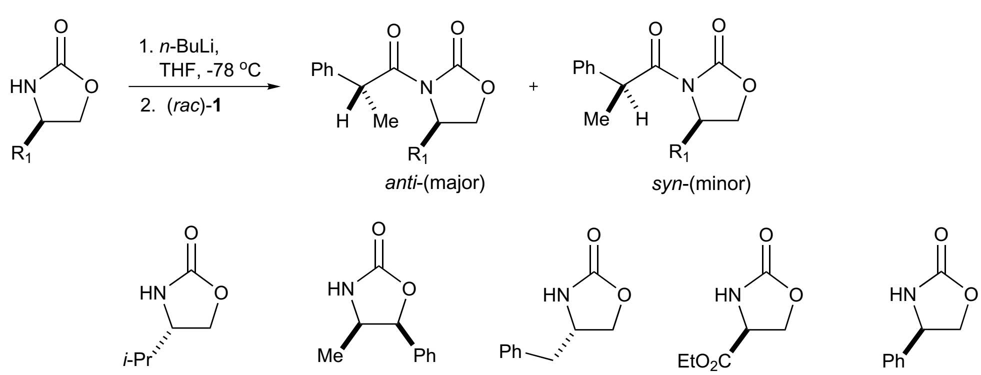
Scheme 2. Kinetic resolution of acid chlorides **1**, **3** and **10** using **8** and **12**.

THF at −78 °C, and found in line with Fukuzawa's reports[11] that a near equimolar mixture of both adducts *anti*- and *syn*-**5** were formed in a 47% yield (Scheme 3). The assignment of stereochemistry was achieved by hydrolyzing each adduct, *anti*- and *syn*-**5**, using a combination of LiOH and H_2O_2[18] to give the corresponding (*S*)- and (*R*)-enantiomers of 2-phenylpropionic acid **10**, respectively (Scheme 3). The absolute stereochemistry of these adducts, *anti*- and *syn*-**5**, was assigned by the comparison of the specific rotation of (*S*)-**10** and (*R*)-**10** with known literature values.[19,20]

In an attempt to gain a better understanding of this process, we next investigated the mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-**1** using a racemic mixture of oxazolidinone *rac*-**4** (Scheme 4). This proved to be moderately diastereoselective, favouring the formation of the *anti*-adduct **5** with 40% diastereoisomeric excess in 60% yield (Scheme 4). The diastereoselectivity was found to decrease with an increase of the enantiomeric excess of the parent oxazolidinone (*S*)-**4**; the use of racemic oxazolidinone **4** gave the highest level of diastereoselectivity (Scheme 4). This type of behaviour was shown to occur with other re-



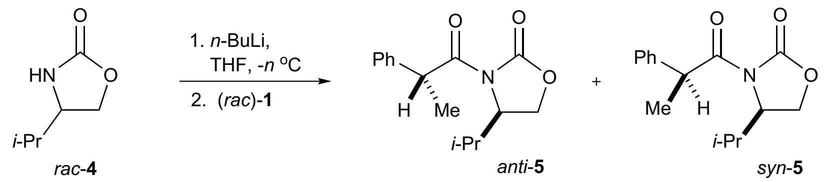
Scheme 3. Hydrolysis of *anti*- and *syn*-adducts **5**.



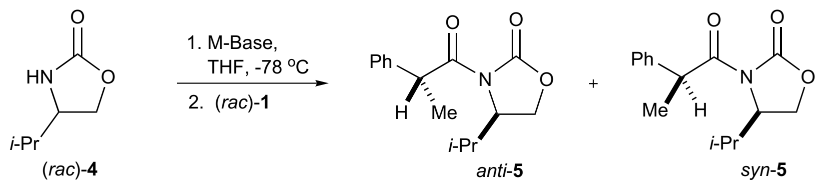
Oxazolidinones		4	14	15	16	17
Using racemic oxazolidinones	*anti*-:*syn*-	**5**; 40% *d.e.* (60%)	**18**; 34% *d.e.* (68%)	**19**; 18% *d.e.* (62%)	**20**; 18% *d.e.* (59%)	**21**; 12% *d.e.* (58%)
Using homochiral oxazolidinones	*anti*-:*syn*-[a]	**5**; 0% *d.e.* (52%)	**18**; 0% *d.e.* (68%)	**19**; 0% *d.e.* (70%)	**20**; 0% *d.e.* (59%)	**21**; 0% *d.e.* (69%)
	anti-:*syn*-[b]	**5**; 4% *d.e.* (47%)	**18**; 0% *d.e.* (70%)	**19**; 4% *d.e.* (70%)	**20**; 0% *d.e.* (69%)	**21**; 14% *d.e.* (71%)

[a]Using 1 equivalent of *rac*-**1**; [b]Using 2 equivalents of *rac*-**1**

Scheme 4. Mutual and kinetic resolution of racemic 2-phenylpropanoyl chloride **1** using oxazolidinones **4**, **14**, **15**, **16** and **17**.

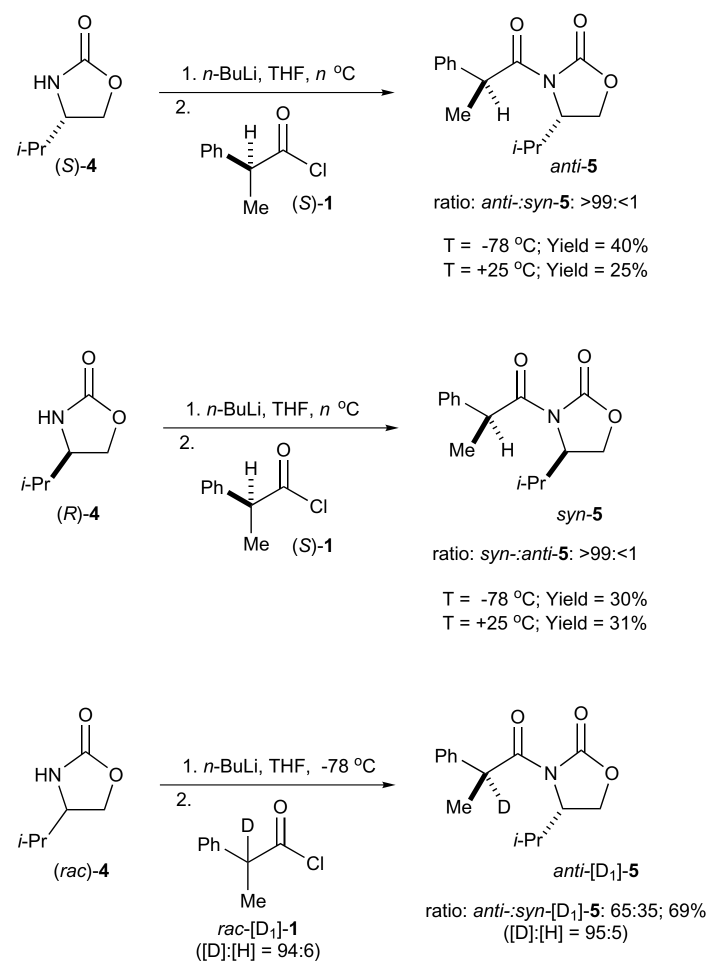


*rac-anti-:syn-***4**	70:30 (60%)	70:30 (60%)	57:43 (65%)	45:55 (52%)	33:67 (49%)	33:67 (50%)
Temperature	-97 °C	-78 °C	-29 °C	0 °C	+25 °C	+50 °C



M-Base	*n*-BuLi	LiHMDS	NaHMDS	KHMDS
*rac-anti-:syn-***5**	70:30 (60%)	64:36 (70%)	34:66 (70%)	38:62 (58%)

Scheme 5. Variation in temperature, metal counter-ion and diastereoselectivity.

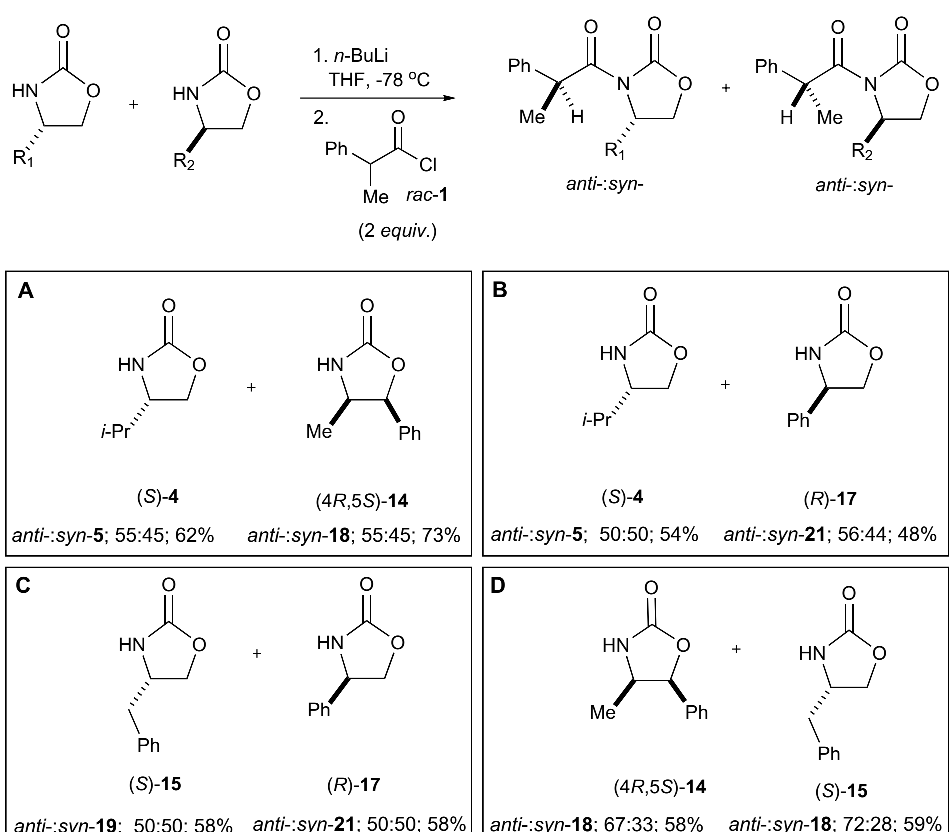


Scheme 6. Stereospecific addition of (*S*)- and (*R*)-**4** to acid chloride (*S*)-**1**.

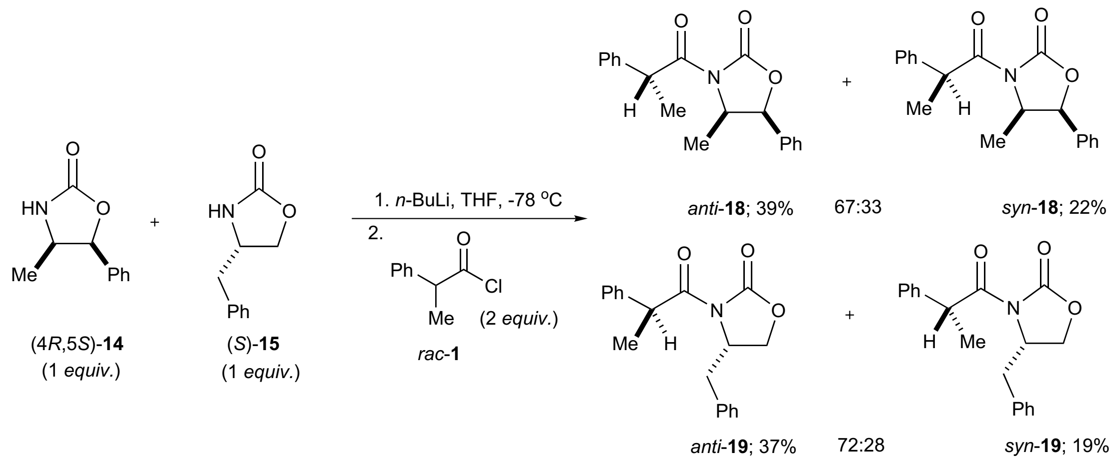
lated oxazoldinones, such as racemic norephedrine, phenylalanine, serine and phenylglycine derived oxazolidinones *rac*-**14**, *rac*-**15**, *rac*-**16** and *rac*-**17**. For these particular cases, they gave better diastereoselectivity than their corresponding enantiomerically pure derivatives (Scheme 4). The exception being the phenylglycine derived oxazolidinone *rac*-**17**, which gave similar levels of diastereocontrol for both the mutual and kinetic resolutions (Scheme 4). The levels of diastereoselectivity and facial selectivity were found to be dependent on the reaction temperature; for example, for oxazolidinone *rac*-**4**, there was a reversal of diastereoselectivity favouring the formation of the *anti*-adduct **5** at a low temperature (−97 °C) through the corresponding *syn*-adduct **5** at a higher temperature (+50 °C) (Scheme 5). The nature of the metal counterion associated with the metallated oxazolidione was also shown to be important in influencing the relative diastereoselectivity; a lithium counterion favoured the formation of the *anti*-adduct **5** (40% de), whereas, a sodium and potassium counter-ion favoured the formation of the corresponding *syn*-adduct **5** with 32% and 24% diastereoisomeric excesses, respectively (Scheme 5).[21]

This nucleophilic addition–elimination process appears to be stereospecific and occurs with retention of configuration; addition of enantiomerically pure lithiated oxazolidinones [derived from the *n*-BuLi addition of (*S*)-**4** and (*R*)-**4**, respectively] to enantiomerically pure 2-phenylpropanoyl chloride (*S*)-**1** at both −78 and +25 °C gave the corresponding diastereoisomerically pure adducts *anti*- and *syn*-**5**, respectively, in 25–40% yields (>98% de) (Scheme 6). The lower yields at room temperature (+25 °C) were presumably due to the competitive deprotonation of the acid chloride *rac*-**1** and subsequent re-formation of the parent oxazolidinone **4**. This competitive deprotonation appears to be slowed sufficiently under the time scale of the reaction by using the *C*(1)-deuterium-labelled acid chloride [D_1]-**1** ([D]:[H] = 94:6), which gave the corresponding *anti*- and *syn*-adducts [D_1]-**5** ([D]:[H] = 95:5) in higher yield (Scheme 6). It is interesting to note, there appears to be little or no primary kinetic isotope effect for the formation of these adducts.

With this information in hand, we next investigated the resolution of 2-phenylpropanoyl chloride *rac*-**1** using an equimolar combination of two complementary enantiomerically pure quasi-enantiomeric oxazolidinones. We chose to study the use of structurally related quasi-enantiomeric oxazolidinones, such as (4*R*,5*S*)-**14** (in **A**) and (*R*)-**17** (in **B**) as potential surrogates for the (*R*)-enantiomer of **4** as this should lead to a comparable diastereoselectivity as with the parent *rac*-**4** (Scheme 7). However, the use of an equimolar mixture of these quasi-enantiomeric oxazolidinones (*S*)-**4** and (4*R*,5*S*)-**14** (in **A**), and (*S*)-**4** and (*R*)-**17** (in **B**) as a mimic for the racemic oxazolidinone **4** gave poorer levels of diastereoselectivity than the original mutual kinetic resolution (Scheme 7). This was presumably due to oxazolidinones (4*R*,5*S*)-**14** and (*R*)-**17** being non-compatible as a complementary enantiomer to (*S*)-**4** within the original mutual kinetic resolution (Scheme 4).



Scheme 7. Parallel resolution of *rac*-**1** using an equimolar combination of quasi-enantiomeric oxazolidinones.

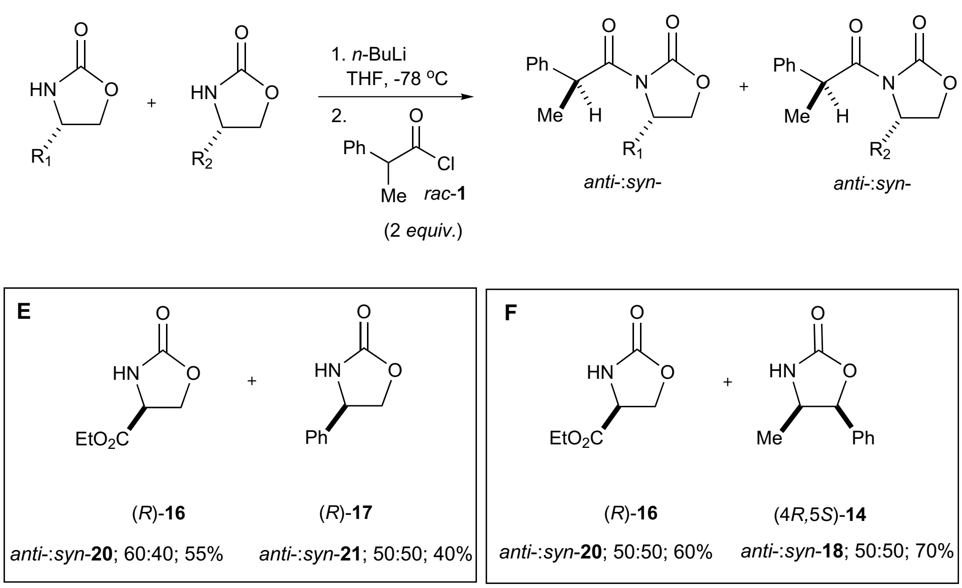


Entry	oxazolidinones		anti-**18**:syn-**18**	anti-**19**:syn-**19**
1		**15**-(*rac*)[a]	*rac*-59:41 (44%)	—
2	**14**-*rac*[a]		—	(*rac*)-67:33 (68%)
3		**15** (*S*-)[b]	52:48 (70%)	—
4	**14**-(4*R*,5*S*)[b]		—	50:50 (70%)
5	**14**-(4*R*,5*S*)-(1 *eq.*) +	**15** (*S*)-(1 *eq.*)[c]	67:33 (58%)	72:28 (59%)
6	**14**-(4*R*,5*S*)-(0.5 *eq.*) +	**15** (*S*)-(1.5 *eq.*)	80:20 (69%)	54:46 (73%)
7	**14**-(4*R*,5*S*)-(1.5 *eq.*) +	**15** (*S*)-(0.5 *eq.*)	64:36 (50%)	78:22 (65%)

[a]Mutual kinetic resolution; [b]Kinetic resolution with 2 equivalents of *rac*-**1**; [c]Parallel kinetic resolution

Scheme 8. Parallel resolution of *rac*-**1** using a combination of quasi-enantiomeric oxazolidinones (4*R*,5*S*)-**14** and (*S*)-**15**.

Probing two further quasi-enantiomeric combinations of oxazolidinones (*S*)-**15** and (*R*)-**17** (in **C**), and (4*R*,5*S*)-**14** and (*S*)-**15** (in **D**) has shown that comparable diastereoselectivity can be achieved using a parallel kinetic resolution approach (Scheme 7). The equimolar combination of oxazolidinones (4*R*,5*S*)-**14** and (*S*)-**15** appears to mirror that of each corresponding racemic pair of oxazolidinones **14** and **15**, respectively (Scheme 7). Interestingly, the diastereo-



Scheme 9. Resolution of *rac*-**1** using a combination of oxazolidinones.

selectivity for these addition processes were found to better than that originally suggested from their individual mutual kinetic resolutions (Scheme 4). The levels of diastereocontrol were evidently dependent on the presence of the chosen surrogate enantiomer for each oxazolidinone, as without it, the overall diastereoselectivity was reduced. In an attempt to enhance the diastereoselectivity by promoting the apparent compatibility between these lithiated oxazolidinones (4*R*,5*S*)-**14** and (*S*)-**15** and the acid chloride *rac*-**1** (in Scheme 7), we chose to use an unequal amount of the parent oxazolidinones (Scheme 8). We argued if a combination of quasi-enantiomers were responsible for improving the diastereocontrol, an increase in stereocontrol might be expected for the product derived from the minor lithiated oxazolidinone, while a decrease in stereocontrol would be expected for the product derived from the complementary major oxazolidinone. Using an excess of the oxazolidinone (4*R*,5*S*)-**14**, the diastereoselectivity of the minor oxazolidinone (*S*)-**15** improved from 44% to 56% de in favour of *anti*-adduct **19** (Scheme 8: entry 7), whereas, using an excess of the other oxazolidinone (*S*)-**15** improved the diastereoselectivity of the minor oxazolidinone (4*R*,5*S*)-**14** from 34% to 60% de in favour of the corresponding *anti*-adduct **18** (Scheme 8: entry 6). For these resolutions both the major components, oxazolidinones (4*R*,5*S*)-**14** (in Scheme 8: entry 7) and oxazolidinones (*S*)-**15** (in Scheme 8: entry 6) gave reduced levels of diastereoselectivity.

We next chose to investigate the resolution of racemic 2-phenylpropanoyl chloride *rac*-**1** using an equimolar combination of oxazolidinones containing the same sense of chirality, such as (*R*)-**16** and (*R*)-**17**, and (*R*)-**16** and (4*R*,5*S*)-**14** to probe their compatibility (Scheme 9). However, these combinations behaved similarly to their parent kinetic resolutions (as illustrated in Scheme 4) giving little to no levels of diastereocontrol (Scheme 9).

3. Conclusion

In conclusion, we have a reported an improved method for the diastereoselective addition of lithiated oxazolidinones to racemic 2-phenylpropanoyl chloride *rac*-**1** by using a parallel kinetic resolution involving complementary (quasi)-enantiomeric Evans oxazolidinones [e.g., (4*R*,5*S*)-**14** and (*S*)-**15**]. We have found that a number of effects, such as the structural nature of the complementary (quasi)-enantiomeric oxazolidinones, choice of metal counter-ions and temperature play an important role of the levels and relative diastereoselectivity; a lithium counter-ion and low temperature promotes the formation of the *anti*-adduct, whereas, a potassium counter-ion and/or high temperature favours the *syn*-adduct. The nearest analogy to this work are the parallel kinetic resolutions reported by Fox,[22] Vedejs[23] and Davies.[24] Fox[22] has shown that a combination of quasi-enantiomeric oxazolidinones can efficiently resolve racemic anhydrides, whereas, Vedejs has elegantly shown the efficient parallel kinetic resolution of 1-phenylethanol using two complementary quasi-enantiomeric chlorocarbonates.[23] By comparison, Davies has shown the use of two quasi-enantiomeric lithium amides to resolve racemic enoates.[24] It is particularly noteworthy that these efficient parallel kinetic resolutions[25] appear to act independently of each other in an equal and opposite stereochemical sense and lead to products with near perfect levels of diastereocontrol.

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 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 rotations were measured using an automatic AA-10 Optical Activity Ltd polarimeter. The levels of *D*-incorporation were determined by a combination of mass, proton and carbon NMR spectra.

4.2. 2-Phenylpropanoyl chloride *rac*-1[26]

2-Phenylpropionic acid **13** (10.0 g, 9.10 ml, 66.5 mmol) was slowly added to neat thionyl chloride (11.9 g, 7.28 ml, 99.8 mmol) and refluxed at 100 °C for 90 min. The solution was distilled (using a short path distillation apparatus at 100–105 °C at 17.5 mmHg) to give the corresponding acid chloride *rac*-**1** (9.64 g, 86%); ν_{max} (film); cm^{-1} 1782 (C=O), δ_H (270 MHz, $CDCl_3$) 7.36–7.28 (5H, m, 5 × CH; Ar), 4.11 (1H, q, *J* 7.1, CH) and 1.59 (3H, d, *J* 7.1, Me); δ_C (100 MHz, $CDCl_3$) 175.9 (C=O), 140.2 (*i*-C; Ph), 129.9, 129.3 and 129.2 (3 × CH; Ph), 57.9 (CH) and 18.6 (Me) (found M(^{35}Cl), 168.0337; C_9H_9ClO requires 168.0336).

4.3. (4*S*)-Isopropyl-3-((2*S*)-phenylpropionyl)oxazolidin-2-one *anti*-5 and (4*S*)-isopropyl-3-((2*R*)-phenylpropionyl)oxazolidin-2-one *syn*-5[8,17a,b,27,28]

n-BuLi (1.55 ml, 2.5 M in hexanes, 3.87 mmol) was added to a stirred solution of oxazolidinone (*S*)-**4** (0.5 g, 3.87 mmol) in THF at −78 °C. After stirring for 1 h, a solution of (±)-2-phenylpropanoyl chloride *rac*-**1** (1.31 g, 7.74 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*- 52:48) of oxazolidinones *anti*- and *syn*-**5**. The residue was purified by flash column chromatography on silica gel eluting with light petroleum (bp 40–60 °C)/diethyl ether (1:1) to give oxazolidinone *anti*-**5** (0.27 g, 27%) as an oil; R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:1)] 0.64; $[\alpha]_D^{20} = +128.9$ (*c* 3.5, $CHCl_3$)[30] {lit.[11] $[\alpha]_D^{20} = +100.6$ (*c* 1.11, $CHCl_3$)},

υ_{max} (film); cm^{-1} 1774 (C=O) and 1701 (C=O); δ_H (250 MHz; $CDCl_3$) 7.38–7.20 (5H, m, 5 × CH; Ph), 5.15 (1H, q, *J* 7.0, PhCH), 4.39–4.33 (1H, m, CHN), 4.18–4.08 (2H, m, CH_2O), 2.50–2.38 (1H, m, $CH(CH_3)_2$), 1.52 (3H, d, *J* 7.0, CH_3CH), 0.92 (3H, d, *J* 7.0, $CH_3^ACHCH_3^B$) and 0.91 (3H, d, *J* 6.9, $CH_3^ACHCH_3^B$); δ_C (62.9 MHz; $CDCl_3$) 174.7 (NC=O), 153.6 (OC=O), 140.4 (*i*-C; Ph), 128.6, 128.2 and 127.2 (3 × CH; Ph), 63.2 (CH_2O), 59.1 (CHN), 43.1 (PhCH), 28.6 ($CH(CH_3)_2$), 19.7 (CH_3), 18.1 (CH_3) and 14.8 (CH_3CH) (found MH^+ 262.1434; $C_{15}H_{20}NO_3^+$ requires 262.1443); *m/z* 262 (30, MH^+), 130 (48, $M-C_9H_8O$) and 105 (100, $M-C_7H_{11}NO_3$); and the oxazolidinone *syn*-**5** (0.20 g, 20%); R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:1)] 0.43; $[\alpha]_D^{20} = -19.8$ (*c* 3.3, $CHCl_3$)[30] {lit.[27] $[\alpha]_D^{20} = -19.2$ (*c* 1.15, $CHCl_3$)}; υ_{max} ($CHCl_3$); cm^{-1} 1774 (C=O) and 1703 (C=O); δ_H (250 MHz; $CDCl_3$) 7.39–7.19 (5H, m, 5 × CH; Ph), 5.14 (1H, q, *J* 6.9, CH_3CHCO), 4.49 (1H, m, CHN), 4.24 (1H, t, *J* 8.9, CH_AH_BO), 4.10 (1H, dd, *J* 8.9 and 3.5, CH_AH_BO), 2.24–2.12 (1H, m, $CH(CH_3)_2$), 1.47 (3H, d, *J* 6.9, CH_3CHCO), 0.79 (3H, d, *J* 7.0, $CH_3^ACHCH_3^B$) and 0.46 (3H, d, *J* 6.9, $^ACH_3CH^BCH_3$); δ_C (62.9 MHz; $CDCl_3$) 174.5 (NC=O), 153.5 (OC=O), 140.5 (*i*-C; Ph), 128.6, 128.1 and 127.2 (3 × CH; Ph), 62.9 (CH_2O), 58.1 (CHN), 43.3 (PhCH), 27.9 ($CH(CH_3)_2$), 18.7 (CH_3), 17.8 (CH_3) and 14.1 (CH_3CH) (found MH^+ 262.1432; $C_{15}H_{20}NO_3^+$ requires 262.1443); *m/z* 262 (30%, MH^+), 130 (48, $M-C_9H_8O$) and 105 (100, $M-C_7H_{11}NO_3$).

4.4. Kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4

In the same way as oxazolidinone **5**, *n*-BuLi (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 50:50) of oxazolidinones *anti*-**5** (0.104 g, 26%) and *syn*-**5** (0.104 g, 26%), which were spectroscopically identical to those previously obtained.

4.5. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4

In the same way as oxazolidinone **5**, *n*-BuLi (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 70:30) of oxazolidinones *anti*-**5** (0.17 g, 42%) and *syn*-**5** (72 mg, 18%), which were spectroscopically identical to those previously obtained.

4.6. (4*R*,5*S*)-4-Methyl-5-phenyl-3-(2*R*-phenylpropionyl)oxazolidin-2-one *anti*-18 and (4*R*,5*S*)-4-methyl-5-phenyl-3-(2*S*-phenylpropionyl)oxazolidin-2-one *syn*-18

In the same way as oxazolidinone **5**, *n*-BuLi (0.91 ml, 2.5 M in hexane, 2.28 mmol), oxazolidinone (4*R*,5*S*)-**14** (0.4 g, 2.28 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.95 g, 5.6 mmol), gave after purification by flash column chromatography eluting with light petroleum (bp 40–60 °C)/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 50:50) of oxazolidinones *anti*-**18** (0.24 g, 35%) as a white solid; mp = 89-92 °C; R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:1)] 0.76; $[\alpha]_D^{20} = -42.7$ (*c* 3, $CHCl_3$);[30] υ_{max} ($CHCl_3$); cm^{-1} 1778 (C=O) and 1697 (C=O); δ_H (250 MHz; $CDCl_3$) 7.44–7.24 (10H, m, 10 × CH; 2 × Ph), 5.49 (1H, d, *J* 7.1, OCHPh), 5.14 (1H, q, *J* 7.1, PhCH), 4.68 (1H, m, CHN), 1.51 (3H, d, *J* 7.1, CH_3CHCO) and 0.94 (3H, d, *J* 6.6, CH_3CHN); δ_C (62.9 MHz; $CDCl_3$) 174.5 (NC=O), 152.6 (OC=O), 140.5 (*i*-C; Ph_A; $PhCHCH_3$), 133.3 (*i*-C; Ph_B; PhCHO), 129.2, 129.1, 128.7, 128.2, 127.3 and 125.6 (6 × CH; Ph_A and Ph_B), 78.7 (OCHPh), 55.5 (CHN), 43.4 (PhCH), 19.3 (CH_3) and 14.6 (CH_3) (found MH^+ 310.1430. $C_{19}H_{20}NO_3^+$ requires 310.1443); *m/z* 310 (31%, MH^+), 178 (9, $M-C_9H_8O$) and 105 (100, $M-C_{11}H_{11}NO_3$); and the oxazolidinones *syn*-**18** (0.24 g, 35%) as a white solid; mp = 121–123 °C; R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:1)] 0.63; $[\alpha]_D^{20} = +105.9$ (*c* 2.6, $CHCl_3$);[30] υ_{max} ($CHCl_3$); cm^{-1} 1774 (C=O) and 1701 (C=O); δ_H (250 MHz; $CDCl_3$) 7.40–7.17 (10H, m, 10 × CH; Ph_A and Ph_B), 5.64 (1H, d, *J* 7.2, OCHPh), 5.08 (1H, q, *J* 7.1, PhCH), 4.82 (1H, m, CHN), 1.51 (3H, d, *J* 7.1, CH_3CHCO) and 0.74 (3H, d, *J* 6.6, CH_3CHN); δ_C (62.9 MHz; $CDCl_3$) 174.3 (NC=O), 152.5 (OC=O), 140.3 (*i*-C; Ph_A; $PhCHCH_3$), 133.5 (*i*-C; Ph_B; PhCHO), 128.9, 128.8, 128.6, 128.1, 127.1 and 125.7 (6 × CH; Ph_A and Ph_B), 78.8 (OCHPh), 54.7 (CHN), 43.6 (PhCH), 19.4 (CH_3) and 14.1 (CH_3) (found MH^+ 310.1460. $C_{19}H_{20}NO_3^+$ requires 310.1443); *m/z* 310 (28%, MH^+), 178 (8, $M-C_9H_8O$) and 105 (100, $M-C_{11}H_{11}NO_3$).

4.7. Kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a racemic oxazolidinone (4*R*,5*S*)-14

In the same way as oxazolidinone **5**, *n*-BuLi (0.68 ml, 2.5 M in hexane, 1.70 mmol), (4*RS*,5*SR*)-oxazolidinone *rac*-**14** (0.30 g, 1.69 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.28 g, 1.69 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 50:50) of oxazolidinones *anti*-**18** (0.18 g, 45%) and *syn*-**18** (0.18 g, 23%), which were spectroscopically identical to those previously obtained.

4.8. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a racemic oxazolidinone (4*R*,5*S*)-14

In the same way as oxazolidinone **5**, *n*-BuLi (0.68 ml, 2.5 M in hexane, 1.70 mmol), (4*RS*,5*SR*)-oxazolidinone *rac*-**14** (0.30 g, 1.69 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.28 g, 1.69 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 67:33) of oxazolidinones *anti*-**18** (0.23 g, 45%) and *syn*-**18** (0.12 g, 23%), which were spectroscopically identical to those previously obtained.

4.9. (4*S*)-Benzyl-3-((2*S*)-phenylpropionyl)oxazolidine-2-one *anti*-19 and (4*S*)-benzyl-3-((2*R*)-phenylpropionyl)oxazolidine-2-one *syn*-19[11,27]

In the same way as oxazolidinone **5**, *n*-BuLi (0.45 ml, 2.5 M in hexane, 1.13 mmol), oxazolidinone (*S*)-**15** (0.2 g, 1.13 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.38 g, 2.26 mmol), gave after purification by flash column chromatography eluting with light petroleum (bp 40–60 °C)/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 52:48) of oxazolidinones *anti*-**19** (0.12 g, 35%) as an oil; R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:1)] 0.66; $[\alpha]_D^{20} = +130.4$ (*c* 1.8, $CHCl_3$) {lit.[11] $[\alpha]_D^{20} = +107.1$ (*c* 1.01, $CHCl_3$)}; ν_{max} ($CHCl_3$); cm^{-1} 1780 (C=O) and 1699 (C=O); δ_H (270 MHz; $CDCl_3$) 7.39–7.21 (10H, m, 10 × CH; 2 × Ph), 5.12 (1H, q, *J* 7.0, PhCH), 4.61–4.54 (1H, m, CHN), 4.12–4.10 (2H, m, CH_2O), 3.35 (1H, dd, *J* 13.1 and 3.2, CH_AH_BPh), 2.80 (1H, dd, *J* 13.1 and 9.8, CH_AH_BPh) and 1.55 (3H, d, *J* 7.0, CH_3CH); δ_C (100 MHz; $CDCl_3$) 174.7 (NC=O), 152.9 (OC=O), 140.3 (*i*-C; Ph_A), 135.4 (*i*-C; Ph_B), 129.5, 129.0, 128.7, 128.1, 127.4 and 127.3 (6 × CH; Ph_A and Ph_B), 65.9 (CH_2O), 55.8 (CHN), 43.2 (PhCH), 38.0 (CH_2Ph) and 19.5 (CH_3) (found MH^+ 310.1442. $C_{19}H_{20}NO_3^+$ requires 310.1443); *m/z* 310 (80%, MH^+), 178 (18, $M-C_9H_8O$), 132 (100, $M-C_{10}H_{12}NO_2$) and 105 (18, $M-C_{11}H_{11}NO_3$); and the oxazolidinone *syn*-**19** (0.12 g, 35%) as a viscous oil; R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:1)] 0.43; $[\alpha]_D^{20} = +2.8$ (*c* 5.5, $CHCl_3$); {lit.[31] $[\alpha]_D^{20} = +2.2$ (*c* 2.8, $CHCl_3$)} {lit.[11] $[\alpha]_D^{20} = +16.1$ (*c* 0.96, $CHCl_3$)}; ν_{max} ($CHCl_3$); cm^{-1} 1775 (C=O) and 1700 (C=O); δ_H (270 MHz; $CDCl_3$) 7.45–6.94 (10H, m, 10 × CH; Ph_A and Ph_B), 5.11 (1H, q, *J* 6.9, PhCH), 4.79–4.70 (1H, m, CHN), 4.18 (1H, t, *J* 8.5, CH_AH_BO), 4.07 (1H, dd *J* 8.5 and 3.2, CH_AH_BO), 3.08 (1H, dd *J* 13.5 and 3.2, CH_AH_BPh), 2.58 (1H, dd, *J* 13.5 and 8.8, CH_AH_BPh) and 1.52 (3H, d, *J* 6.9, CH_3CH); δ_C (100 MHz; $CDCl_3$) 174.5 (NC=O), 153.0 (OC=O), 140.2 (*i*-C; Ph_A), 135.0 (*i*-C; Ph_B), 129.4, 128.8, 128.6, 128.3, 127.3 and 127.2 (6 × CH; Ph_A and Ph_B), 65.8 (CH_2O), 54.9 (CHN), 43.2 (PhCH), 37.4 (CH_2) and 19.2 (CH_3) (found MH^+ 310.1438. $C_{19}H_{20}NO_3^+$ requires 310.1443); *m/z* 310 (80%, MH^+), 178 (15, $M-C_9H_8O$), 132 (100, $M-C_{10}H_{12}NO_2$) and 105 (15, $M-C_{11}H_{11}NO_3$).

4.10. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a racemic lithiated oxazolidinone *rac*-15

In the same way as oxazolidinone **5**, *n*-BuLi (0.45 ml, 2.5 M in hexane, 1.12 mmol), oxazolidinone *rac*-**15** (0.20 g, 1.13 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.19 g, 1.13 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 59:41) of oxazolidinones *anti*-**19** (0.126 g, 36%) and *syn*-**19** (91 mg, 26%), which were spectroscopically identical to those previously obtained.

4.11. Kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a racemic lithiated oxazolidinone *rac*-15

In the same way as oxazolidinone **5**, *n*-BuLi (0.45 ml, 2.5 M in hexane, 1.12 mmol), oxazolidinone *rac*-**15** (0.20 g, 1.13 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.19 g, 1.13 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 50:50) of oxazolidinones *anti*-**19** (0.122 g, 35%) and *syn*-**19** (0.122 g, 35%), which were spectroscopically identical to those previously obtained.

4.12. Synthesis of ethyl (4*S*,2*R*)-2-oxa-3-(2′-phenylpropionyl)oxazolidin-4-carboxylate *anti*-20 and ethyl (4*S*,2*S*)-2-oxa-3-(2′-phenylpropionyl)oxazolidin-4-carboxylate *syn*-20

In the same way as oxazolidinone **5**, *n*-BuLi (2.01 ml, 2.5 M in hexane, 5.03 mmol), oxazolidinone (*S*)-**16** (0.8 g, 5.03 mmol) and (±)-2-phenyl propanoyl chloride *rac*-**1** (1.69 g, 10.1 mmol), gave a mixture of two diastereoisomers [ratio 50:50: *anti*-:*syn*-] of oxazolidinones **20**. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum (bp 40–60 °C)/diethyl ether (7:3) the (*S*,*R*)-oxazolidinone *anti*-**20** (0.51 g, 35%) as an oil; R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:1)] 0.42; $[\alpha]_D^{20} = -135.8$ (*c* 4.5, $CHCl_3$); ν_{max} ($CHCl_3$); cm^{-1} 1794 (C=O), 1747 (C=O) and 1705 (C=O); δ_H (270 MHz; $CDCl_3$) 7.33–7.20 (5H, m, 5 × CH; Ph), 5.10 (1H, q, *J* 7.0, PhCH), 4.77 (1H, dd, *J* 9.4 and 3.7, CHN), 4.38 (1H, t, *J* 9.4, CH_AH_BO), 4.31–4.21 (3H, m, CH_AH_BO and CH_2CH_3), 1.50 (3H, d, *J* 7.0, CH_3CH) and 1.30 (3H, t, *J* 7.2, CH_3CH_2); δ_C (62.9 MHz; $CDCl_3$) 174.5 (NC=O), 168.7 (CC=O), 152.1 (OC=O), 140.0 (*i*-C; Ph), 128.7, 128.3 and 127.4 (3 × CH; Ph), 64.3 (CH_2O), 62.6 (CH_2O), 55.9 (CHN), 43.0 (PhCH), 19.3 (CH_3CH) and 14.1 (CH_3CH_2) (found MH^+, 292.1195; $C_{15}H_{18}NO_5^+$ requires 292.1185) and the (*S*,*S*)-oxazolidinone *syn*-**20** (0.49 g, 34%) as a white powder; mp = 97–99 °C; R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:1)] 0.30; $[\alpha]_D^{20} = +17.2$ (*c* 2.2, $CHCl_3$); ν_{max} ($CHCl_3$); cm^{-1} 1793 (C=O), 1747 (C=O) and 1705 (C=O); δ_H (270 MHz; $CDCl_3$) 7.40–7.20 (5H, m, 5 × CH; Ph), 5.03 (1H, q, *J* 7.0, PhCH), 4.94 (1H, dd, *J* 9.3 and 4.9, CHN), 4.52 (1H, t, *J* 9.3, CH_AH_BO), 4.23 (1H, dd, *J* 9.3 and 4.9, CH_AH_BO), 4.11 (2H, q, *J* 7.2, CH_2CH_3), 1.48 (3H, d, *J* 7.0, CH_3CH) and 1.11 (3H, t, *J* 7.2, CH_3CH_2); δ_C (62.9 MHz; $CDCl_3$) 174.3 (NC=O), 168.1 (CC=O), 152.0 (OC=O), 139.8 (*i*-C; Ph), 128.5, 128.2 and 127.2 (3 × CH; Ph), 64.3 (CH_2O), 62.4 (CH_2O), 55.7 (CHN), 43.2 (PhCH), 19.4 (CH_3) and 13.9 (CH_3) (found MH^+, 292.1195; $C_{15}H_{18}NO_5^+$ requires 292.1185).

4.13. Kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-16

In the same way as oxazolidinone **5**, *n*-BuLi (0.50 ml, 2.5 M in hexane, 1.25 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.25 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.21 g, 1.25 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 50:50) of oxazolidinones *anti*-**20** (0.105 g, 29%) and *syn*-**20** (0.109 g, 30%), which were spectroscopically identical to those previously obtained.

4.14. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-16

In the same way as oxazolidinone **5**, *n*-BuLi (0.50 ml, 2.5 M in hexane, 1.25 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.25 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.21 g, 1.25 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 59:41) of oxazolidinones *anti*-**20** (0.128 g, 35%) and *syn*-**20** (87 mg, 24%), which were spectroscopically identical to those previously obtained.

4.15. Synthesis of (4*R*,2*R*)-4-phenyl-3-(2′-phenylpropionyl)oxazolidin-2-one *anti*-21 and (4*R*,2*S*)-4-phenyl-3-(2′-phenylpropionyl)oxazolidin-2-one *syn*-21[11,17a,b,27,28]

In the same way as oxazolidinone **5**, *n*-BuLi (0.49 ml, 2.5 M in hexane, 1.23 mmol), oxazolidinone (*R*)-**17** (0.2 g, 1.23 mmol) and (±)-2-phenyl propanoyl chloride *rac*-**1** (0.41 g, 2.45 mmol), gave a mixture of two diastereoisomers [ratio (57/43:*anti*-/*syn*-)] of oxazolidinone **21**. The crude residue was purified by flash column chromatography on silica gel eluting with light petroleum (bp 40–60 °C)/ether (7:3) the (*R*,*R*)-oxazolidinone *anti*-**21** (0.14 g, 38%) as a white solid; mp = 158–160 °C; R_F [light petroleum (bp 40–60 °C)/ether (1:1)] 0.58; $[\alpha]_D^{20} = -180.5$ (*c* 1.52, $CHCl_3$) {lit.[29] $[\alpha]_D^{20} = -163.2$ (*c* 0.1, $CHCl_3$)}; ν_{max} ($CHCl_3$); cm^{-1} 1780 (C=O) and 1700 (C=O); δ_H (270 MHz; $CDCl_3$) 7.39–7.26 (10H, m, 10 × CH; 2 × Ph), 5.32 (1H, dd, *J* 8.8 and 3.2, CHN), 5.11 (1H, q, *J* 7.2, PhCH), 4.55 (1H, t, *J* 8.8, CH_AH_BO), 4.21 (1H, dd, *J* 8.8 and 3.2, CH_AH_BO) and 1.40 (3H, d, *J* 7.2, CH_3CH); δ_C (62.9 MHz; $CDCl_3$) 174.1 (NC=O), 152.9 (OC=O), 140.2 (*i*-C; Ph_A), 139.4 (*i*-C; Ph_B), 129.3, 128.7, 128.6, 128.2, 127.3 and 125.8 (6 × CH; Ph_A and Ph_B), 69.7 (CH_2O), 58.1 (CHN), 43.2 (PhCH) and 19.4 (CH_3) (found MH^+, 296.1282; $C_{18}H_{18}NO_3^+$ requires 296.1287); and the (*R*,*S*)-oxazolidinone *syn*-**21** (0.12 g, 33%) as a white solid; mp = 140–142 °C; R_F [light petroleum (bp 40–60 °C)/ether (1:1)] 0.42; ν_{max} ($CHCl_3$); cm^{-1} 1778 (C=O) and 1701 (C=O); $[\alpha]_D^{20} = +88.5$ (*c* 4.0, $CHCl_3$); {lit.[29] $[\alpha]_D^{20} = +143.4$ (*c* 0.5 $CHCl_3$)}; δ_H (270 MHz; $CDCl_3$) 7.29–7.21 (10H, m, 10 × CH; 2 × Ph), 5.45 (1H, dd, *J* 9.0 and 5.1, CHN), 5.09 (1H, q, *J* 6.9, PhCH), 4.63 (1H, t, *J* 9.0, CH_AH_BO), 4.08 (1H, dd, *J* 9.0 and 5.1, CH_AH_BO) and 1.39 (3H, d, *J* 6.9, CH_3CH); δ_C (62.9 MHz; $CDCl_3$) 173.7 (NC=O), 153.2 (OC=O), 139.9 (*i*-C; Ph_A), 138.3 (*i*-C; Ph_B), 128.9, 128.7, 128.5, 128.2, 127.1 and 125.9 (6 × CH; Ph_A and Ph_B), 69.6 (CH_2O), 57.9 (CHN), 43.9 (PhCH) and 18.6 (CH_3) (found MH^+, 296.1286; $C_{15}H_{18}NO_3^+$ requires 296.1287).

4.16. Kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-21

In the same way as oxazolidinone **5**, *n*-BuLi (0.48 ml, 2.5 M in hexane, 1.22 mmol), oxazolidinone (*R*)-**17** (0.2 g, 1.22 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.20 g, 1.22 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 50:50) of oxazolidinones *anti*-**5** (0.122 g, 34%) and *syn*-**5** (0.125 g, 35%), which were spectroscopically identical to those previously obtained.

4.17. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-21

In the same way as oxazolidinone **5**, *n*-BuLi (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 56:44) of oxazolidinones *anti*-**5** (0.116 g, 32%) and *syn*-**5** (93 mg, 26%), which were spectroscopically identical to those previously obtained.

4.18. Temperature study

4.18.1. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4 at −97 °C. In the same way as oxazolidinone **5**, *n*-BuLi (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol) at −97 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 70:30) of oxazolidinones *anti*- and *syn*-**5** (0.16 g, 40%), which were spectroscopically identical to those previously obtained.

4.18.2. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4 at −29 °C. In the same way as oxazolidinone **5**, *n*-BuLi (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol) at −29 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 57:43) of oxazolidinones *anti*- and *syn*-**5** (0.26 g, 65%), which were spectroscopically identical to those previously obtained.

4.18.3. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4 at 0 °C. In the same way as oxazolidinone **5**, *n*-BuLi (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol) at 0 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 45:55) of oxazolidinones *anti*- and *syn*-**5** (0.21 g, 52%), which were spectroscopically identical to those previously obtained.

4.18.4. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4 at 25 °C. In the same way as oxazolidinone **5**, *n*-BuLi (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol) at 25 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 33:67) of oxazolidinones *anti*- and *syn*-**5** (0.20 g, 49%), which were spectroscopically identical to those previously obtained.

4.18.5. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4 at 50 °C. In the same way as oxazolidinone **5**, *n*-BuLi (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol) at 50 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 33:67) of oxazolidinones *anti*- and *syn*-**5** (0.20 g, 49%), which were spectroscopically identical to those previously obtained.

4.19. Deprotonation with metal amides

4.19.1. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4 using LiHMDS. In the same way as oxazolidinone **5**, LiHMDS (1.55 ml, 1 M in THF, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol) at 50 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 64:36) of oxazolidinones *anti*- and *syn*-**5** (0.28 g, 70%), which were spectroscopically identical to those previously obtained.

4.19.2. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4 using NaHMDS. In the same way as oxazolidinone **5**, NaHMDS (0.77 ml, 2 M in THF, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol) at 50 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 34:66) of oxazolidinones *anti*- and *syn*-**5** (0.28 g, 70%), which were spectroscopically identical to those previously obtained.

4.19.3. Mutual kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 with oxazolidinone *rac*-4 using KHMDS. In the same way as oxazolidinone **5**, KHMDS (3.1 ml, 0.5 M in THF, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.26 g, 1.54 mmol) at 50 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 38:62) of oxazolidinones *anti*- and *syn*-**5** (0.23 g, 70%), which were spectroscopically identical to those previously obtained.

4.20. Configurational stability study

4.20.1. Addition of propanoyl chloride (*S*)-1 (derived from enantiomerically pure 2-phenylpropanoic acid) to the oxazolidinone (*S*)-4 at −78 °C. In the same way as oxazolidinone **5**, *n*-BuLi (0.31 ml, 2.5 M in hexane, 0.77 mmol), oxazolidinone (*S*)-**4** (0.1 g, 0.77 mmol) and 2-phenylpropanoyl chloride (*S*)-**1** (0.13 g, 0.77 mmol) at −78 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3) the diastereoisomerically (*S*,*S*)-oxazolidinone *anti*-**5** (80 mg, 40%) as an oil, which was spectroscopically identical to that previously obtained. The presence of a single diastereoisomeric adduct was determined by 400 MHz ^{1}H NMR spectroscopy of the crude and purified samples.

4.20.2. Addition of propanoyl chloride (*S*)-1 (derived from enantiomerically pure 2-phenylpropanoic acid) to the oxazolidinone (*R*)-4 at −78 °C. In the same way as oxazolidinone **5**, *n*-BuLi (0.31 ml, 2.5 M in hexane, 0.77 mmol), oxazolidinone (*R*)-**4** (0.1 g, 0.77 mmol) and 2-phenylpropanoyl chloride (*S*)-**1** (0.13 g, 0.77 mmol) at −78 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3) the diastereoisomerically (*R*,*S*)-oxazolidinone *syn*-**5** (60 mg, 30%) as an oil, which was spectroscopically identical to that previously obtained. The presence of a single diastereoisomeric adduct was confirmed by 400 MHz ^{1}H NMR spectroscopy of the crude and purified samples.

4.20.3. Addition of propanoyl chloride (*S*)-1 (derived from enantiomerically pure 2-phenylpropanoic acid) to the oxazolidinone (*S*)-4 at 25 °C. In the same way as oxazolidinone **5**, *n*-BuLi (0.31 ml, 2.5 M in hexane, 0.77 mmol), oxazolidinone (*S*)-**4** (0.1 g, 0.77 mmol) and 2-phenylpropanoyl chloride (*S*)-**1** (0.13 g, 0.77 mmol) at 25 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3) the diastereoisomerically (*S*,*S*)-oxazolidinone *anti*-**5** (59 mg, 25%) as an oil, which was spectroscopically identical to that previously obtained. The presence of a single diastereoisomeric adduct was confirmed by 400 MHz ^{1}H NMR spectroscopy of the crude and purified samples.

4.20.4. Addition of propanoyl chloride (*S*)-1 (derived from enantiomerically pure 2-phenylpropanoic acid) to the oxazolidinone (*R*)-4 at 25 °C. In the same way as oxazolidinone **5**, *n*-BuLi (0.31 ml, 2.5 M in hexane, 0.77 mmol), oxazolidinone (*R*)-**4** (0.1 g, 0.77 mmol) and 2-phenylpropanoyl chloride (*S*)-**1** (0.13 g, 0.77 mmol) at 25 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), the diastereoisomerically (*R*,*S*)-oxazolidinone *syn*-**5** (62 mg, 31%) as an oil, which was spectroscopically identical to that previously obtained. The presence of a single diastereoisomeric adduct was confirmed by 400 MHz ^{1}H NMR spectroscopy of the crude and purified samples.

4.21. Isotope study

4.21.1. Mutual kinetic resolution of 2-deuterio-2-phenylpropanoyl chloride *rac*-[D_1]-1 with oxazolidinone *rac*-4. In the same way as oxazolidinone **5**, *n*-BuLi (0.62 ml, 2.5 M in hexane, 1.55 mmol), oxazolidinone *rac*-**4** (0.2 g, 1.54 mmol) and (±)-2-deuterio-2-phenylpropanoyl chloride *rac*-[D_1]-**1** ([D]:[H] = 94:6—determined by ^{1}H NMR spectroscopy and low resolution mass spectrometry) (0.26 g, 1.54 mmol) at 50 °C, gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 65:35) of oxazolidinones *anti*-[D_1]-**5** ([D]:[H] = 95:5) (0.10 g, 25%) as a viscous oil; R_F [light petroleum (40–60 °C)/diethyl ether (1:1)] 0.57; ν_{max} (CH_2Cl_2); cm^{-1} 2306 (br, C–D), 1779 (C=O) and 1698 (C=O); δ_H (270 MHz; $CDCl_3$) 7.39–7.15 (5H, m, 5 × CH; Ph), 435 (1H, m, CHN), 4.16–4.08 (2H, m, CH_2O), 2.43 (1H, m, CH(CH_3)$_2$), 1.50 (3H, s, $CDCH_3$), 0.91 (3H, d, *J* 6.9, $CHCH_3^ACH_3^B$) and 0.90 (3H, d, *J* 6.9, $CHCH_3{}^ACH_3{}^B$); δ_C (100 MHz; $CDCl_3$) 173.6 (NC=O), 152.6 (OC=O), 139.1 (*i*-C; Ph), 127.6, 127.2 and 126.2 (3 × CH; Ph), 62.0 (CH_2O), 57.9 (CHN), 41.6 (1 C, t, $^1J_{C,D}$ 20.3, PhCD), 27.4 (CH(CH_3)$_2$), 18.5 (CH_3), 16.9 (CH_3) and 13.6 (CH_3) (found M^+, 262.1422; $C_{15}H_{18}DNO_3{}^+$ requires 262.1427); and *syn*-[D_1]-**5** ([D]:[H] = 95:5) (0.18 g, 44%); R_F [light petroleum (40–60 °C)/diethyl ether (1:1)] 0.50; mp 50–53 °C; ν_{max} (CH_2Cl_2); cm^{-1} 2306 (br, C–D), 1778 (C=O) and 1698 (C=O); δ_H (270 MHz; $CDCl_3$) 7.39–7.17 (5H, m, 5 × CH; Ph), 4.51–4.45 (1H, m, CHN), 4.23 (1H, t, *J* 8.9, CH_AH_BO), 4.09 (1H, dd, *J* 8.9 and 3.6, CH_AH_BO), 2.16 (1H, m, CH(CH_3)$_2$), 1.45 (3H, s, $CDCH_3$), 0.80 (3H, d, *J* 6.9, $CHCH_3^ACH_3^B$) and 0.45 (3H, d, *J* 6.9, $CHCH_3^ACH_3^B$); δ_C (100 MHz; $CDCl_3$) 174.5 (NC=O), 153.5 (OC=O), 140.4 (*i*-C; Ph), 128.6, 128.0 and 127.3 (3 × CH; Ph), 62.9 (CH_2O), 58.2 (CHN), 43.0 (1 C, t, $^1J_{C,D}$ 20.3, PhCD), 29.7 (CH(CH_3)$_2$), 18.6 (CH_3), 17.8 (CH_3) and 14.0 (CH_3) (found MH^+, 263.1498; $C_{15}H_{19}DNO_3{}^+$ requires 263.1505).

4.22. Parallel kinetic resolutions

4.22.1. Parallel kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a quasi-enantiomeric combination of oxazolidinones (4*R*,5*S*)-14 and (*S*)-15 (ratio 1:1). In the same way as oxazolidinone **5**, *n*-BuLi (0.45 ml, 2.5 M in hexane, 1.12 mmol), oxazolidinone (4*R*,5*S*)-**14** (0.1 g, 0.56 mmol) and (*S*)-**15** (0.1 g, 0.56 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.19 g, 1.13 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 67:33) of oxazolidinones *anti*-**18** (68 mg, 39%) and *syn*-**18** (33 mg, 19%) [derived from (4*R*,5*S*)-**14**] and a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 72:28) of oxazolidinones *anti*-**19** (74 mg, 44%) and *syn*-**19** (26 mg, 14%) [derived from (*S*)-**15**], which were spectroscopically identical to those obtained previously.

4.22.2. Parallel kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a quasi-enantiomeric combination of oxazolidinones (4*R*,5*S*)-14 and (*S*)-15 (relative ratio 1:3). In the same way as oxazolidinone **5**, *n*-BuLi (0.61 ml, 2.5 M in hexane, 1.52 mmol), oxazolidinone (4*R*,5*S*)-**14** (66 mg, 0.38 mmol) and (*S*)-**15** (0.2 g, 1.13 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.25 g, 1.50 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 80:20) of oxazolidinones *anti*-**18** (64 mg, 55%) and *syn*-**18** (16 mg, 14%) (derived from (4*R*,5*S*)-**14**) and a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 54:46) of oxazolidinones *anti*-**19** (0.14 g, 41%) and *syn*-**19** (0.11 g, 32%) (derived from (*S*)-**15**), which were spectroscopically identical to those obtained previously.

4.22.3. Parallel kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a quasi-enantiomeric combination of oxazolidinones (4*R*,5*S*)-14 and (*S*)-15 (relative ratio 3:1). In the same way as oxazolidinone **5**, *n*-BuLi (0.61 ml, 2.5 M in hexane, 1.52 mmol), oxazolidinone (4*R*,5*S*)-**14** (0.2 g, 1.13 mmol) and (*S*)-**15** (66 mg, 0.38 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.25 g, 1.50 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 64:36) of oxazolidinones *anti*-**18** (0.11 g, 32%) and *syn*-**18** (66 mg, 19%) (derived from (4*R*,5*S*)-**14**) and a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 78:22) of oxazolidinones *anti*-**19** (61 mg, 52%) and *syn*-**19** (16 mg, 13%) (derived from (*S*)-**15**), which were spectroscopically identical to that previously obtained.

4.22.4. Parallel kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a quasi-enantiomeric combination of oxazolidinones and (*S*)-4 and (4*R*,5*S*)-14 (ratio 1:1). In the same way as oxazolidinone **5**, *n*-BuLi (0.45 ml, 2.5 M in hexane, 1.12 mmol), oxazolidinone (*S*)-**4** (72 mg, 0.56 mmol) and (4*R*,5*S*)-**14** (0.1 g, 0.56 mmol) and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.19 g, 1.13 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 55:45) of oxazolidinones *anti*-**5** (50 mg, 34%) and *syn*-**5** (41 mg, 28%) [derived from (*S*)-**4**], and a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 55:45) of oxazolidinones *anti*-**18** (69 mg, 40%) and *syn*-**18** (57 mg, 33%) [derived from (4*R*,5*S*)-**14**], which were spectroscopically identical to those obtained previously.

4.22.5. Parallel kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a quasi-enantiomeric combination of oxazolidinones (*S*)-4 and (*R*)-17 (ratio 1:1). In the same way as oxazolidinone **5**, *n*-BuLi (0.48 ml, 2.5 M in hexane, 1.22 mmol), oxazolidinone (*S*)-**4** (78 mg, 0.61 mmol) and (*R*)-**17** (0.1 g, 0.61 mmol), and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.21 g, 1.22 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 50:50) of oxazolidinones *anti*-**5** (44 mg, 28%) and *syn*-**5** (44 mg, 28%) [derived from (*S*)-**4**] and a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 56:44) of oxazolidinones *anti*-**21** (48 mg, 27%) and *syn*-**21** (38 mg, 21%) [derived from (*R*)-**17**], which were spectroscopically identical to those obtained previously.

4.22.6. Parallel kinetic resolution of 2-phenylpropanoyl chloride *rac*-1 using a quasi-enantiomeric combination of oxazolidinones (*S*)-15 and (*R*)-17 (ratio 1:1). In the same way as oxazolidinone **5**, *n*-BuLi (0.45 ml, 2.5 M in hexane, 1.12 mmol), oxazolidinone (*S*)-**15** (0.1 g, 0.56 mmol) and (*R*)-**17** (91.4 g, 0.56 mmol), and (±)-2-phenylpropanoyl chloride *rac*-**1** (0.19 g, 1.13 mmol), gave after purification by flash column chromatography eluting with light petroleum/diethyl ether (7:3), a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 50:50) of oxazolidinones *anti*-**19** (50 mg, 29%) and *syn*-**19** (50 mg, 29%) [derived from (*S*)-**15**] and a separable diastereoisomeric mixture (*anti*-:*syn*-: ratio 50:50) of oxazolidinones *anti*-**21** (48 mg, 29%) and *syn*-**21** (48 mg, 29%) [derived from (*R*)-**17**], which were spectroscopically identical to those obtained previously.

4.23. Hydrolysis of oxazolidione adducts *anti*-5 and *syn*-5

4.23.1. (−)-2-Phenylpropionic acid (*R*)-13. Lithium hydroxide monohydrate (27 mg, 0.65 mmol) was slowly added to a stirred solution of oxazolidinone *syn*-**5** (83 mg, 0.32 mmol) and hydrogen peroxide (22 mg, 0.65 mmol, 30%/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 (*S*)-**4** (39 mg, 95%) as a white solid. The aqueous phase was acidified using HCl (3 M HCl) until the pH = 3, and extracted with diethylether (3 × 10 ml). The combined organic phases were dried over $MgSO_4$ and evaporated under reduced pressure to give (−)-2-phenylpropionic acid (*R*)-**13** (47.5 mg, 99%) as an oil; $[\alpha]_D^{20} = -71.2$ (*c* 0.66, $CHCl_3$), {lit.[19] $[\alpha]_D^{20} = -72.0$}; ν_{max} ($CHCl_3$); cm^{-1} 1706 (C=O); R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:9)] 0.5; δ_H (250 MHz; $CDCl_3$) 7.45–6.98 (5H, m, 5 × CH; Ph), 3.75 (1H, q, *J* 7.2, PhCH) and 1.5 (3H, d, *J* 7.2, CH_3CH); δ_C (67.9 MHz; $CDCl_3$) 181.4 (C=O), 139.9 (*i*-C; Ph), 128.9, 127.8 and 127.6 (3 × CH; Ph), 45.6 (PhCH) and 18.3 (CH_3) (found MH^+ 151.0750. $C_9H_{11}NO_2{}^+$ requires 151.0759); *m*/*z* 151 (25%, MH^+) and 105 (100, M−CH_2O_2).

4.23.2. (+)-2-Phenylpropionic acid (*S*)-13. In the same way as oxazolidinone *syn*-**5**, oxazolidinone *anti*-**5** (83 mg, 0.32 mmol), lithium hydroxide monohydrate (27.1 mg, 0.65 mmol) and hydrogen peroxide (22 mg, 0.65 mmol, 30%/w), gave after extraction the recovered oxazolidinone (*S*)-**4** (39 mg, 95%) as a white solid; and (+)-2-phenylpropionic acid (*S*)-**13** (47.5 mg, 99%) as an oil; R_F [light petroleum (bp 40–60 °C)/diethyl ether (1:9)] 0.5; $[\alpha]_D^{20} = +71.5$ (*c* 0.64, $CHCl_3$), {lit.[19] $[\alpha]_D^{20} = +72.0$}; ν_{max} ($CHCl_3$); cm^{-1} 1706 (C=O); δ_H (270 MHz; $CDCl_3$) 7.45–6.98 (5H, m, 5 × CH; Ph), 3.75 (1H, q, *J* 7.2, PhCH) and 1.5 (3H, d, *J* 7.2, CH_3CH); δ_C (67.9 MHz; $CDCl_3$) 181.4 (C=O), 139.9 (*i*-C; Ph), 128.9, 127.8 and 127.6 (3 × CH; Ph), 45.6 (PhCH) and 18.3 (CH_3) (found MH^+ 151.0753. $C_9H_{11}NO_2{}^+$ requires 151.0759); *m*/*z* 151 (30%, MH) and 105 (100, M−CH_2O_2).

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20. The enantiomeric purity (>98% ee) was determined by the formation of its corresponding pentafluorophenyl ester and subsequent chemical derivatization with oxazolidinone (*R*)-**17**. For a representative reaction see Ref. 17b.
21. Interesting, by the addition of a sodiated oxazolidinone (derived from the deprotonation of *rac*-**4** with NaHMDS) to *rac-anti*-**5** (de = 99%) at −78 °C for 2 h lowered the diastereoisomeric excess to 84% de [*rac-anti*-**5**:*syn*-**5** = 92:8]. By comparison, the addition of the same sodiated oxazolidinone to *rac-syn*-**5** (de >99%) under identical conditions gave no measurable change in diastereoisomeric excess. A related stereochemical change has previously been reported; see: Evans, D. A.; Faul, M. M.; Colombo, L.; Bisaha, J.; Clardy, J.; Cherry, D. *J. Am. Chem. Soc.* **1992**, *114*, 5977–5985.
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