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Stereoselective functionalisation of SuperQuat enamides: asymmetric synthesis of homochiral 1,2-diols and α-benzyloxy carbonyl compounds

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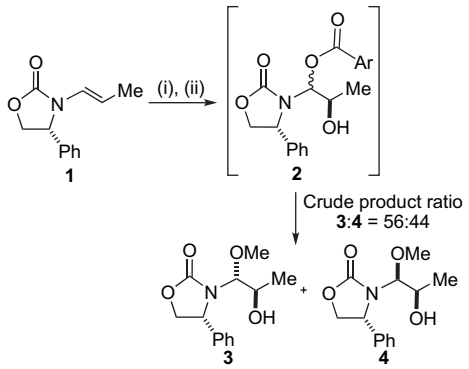
ABSTRACT

Homochiral (*E*)- and (*Z*)-enamides derived from SuperQuat (*S*)-4-phenyl-5,5-dimethyl-oxazolidin-2-one undergo highly diastereoselective epoxidation upon treatment with dimethyldioxirane. Subsequent epoxide opening with *meta*-chlorobenzoic acid proceeds via a stereoselective S_N1-type process, with retention of configuration, to give the corresponding 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives. Treatment of the SuperQuat enamides with *m*CPBA effects this two-step transformation in one pot. Reductive cleavage of the isolated 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives (≥96% de) generates homochiral 1,2-diols in ≥96% ee. Alternatively, regioselective lithiation of the enamide at C(1′) with ^{t}BuLi followed by reaction with an aromatic aldehyde and in situ O-benzylation generates a 1′-(benzyloxy-aryl-methyl) substituted enamide with high diastereoselectivity. Subsequent oxidative cleavage of the enamide C=C bond with $NaIO_4/RuCl_3$ followed by methanolysis of the resultant *N*-acyl fragment furnishes an *O*-benzyl protected α-hydroxy methyl ester in high ee.

1. Introduction

Homochiral 1,2-diols and α-hydroxy carbonyl compounds are valuable building blocks in the synthesis of biologically active compounds and natural products; the motif occurs in numerous synthetic intermediates[1] and is readily amenable to manipulation.[2] The utility of the 1,2-diol motif has ensured that a multitude of methods have been developed for its synthesis in both racemic and homochiral forms,[3] with the oxidation of olefins having proven to be a popular and versatile transformation.[4] Synthetic investigations concerning the oxidative functionalisation of enamines and enamides[5] with either dimethyldioxirane (DMDO) or *m*CPBA have demonstrated that oxidation occurs selectively at the C=C bond rather than at the nitrogen atom. Although isolation of the epoxides formed upon oxidation of enamines is generally difficult due to dimerisation,[6] N-acylation has been shown to stabilise the corresponding enamide epoxides, enabling their detection via spectroscopic methods.[7] The oxidative functionalisation of enamides derived from the Evans auxiliary was initially demonstrated by Hsung et al.,[5a] whereupon treatment of **1** with *m*CPBA followed by HCl in MeOH gave a 56:44 mixture of **3** and **4** in 80% yield. This stereochemical outcome was proposed to be a result of epoxidation of **1** in a highly selective manner on the face opposite to the stereodirecting group of the auxiliary (Scheme 1). Subsequently, Adam et al.[5b,c] investigated the oxidation of a range of enamides derived from the Evans auxiliary with DMDO and *m*CPBA. For instance, enamide **5** reacted with DMDO to give epoxide **6** in 84% de. Subsequent acidic hydrolysis followed by reduction gave terminal 1,2-diol **8** in 84% ee. Alternatively, treatment of **5** with *m*CPBA was reported to generate **7** in 84% de, with the stereochemistry of **7** being assigned on the assumption of ring opening of epoxide



Scheme 1. Reagents and conditions: (i) *m*CPBA, DCM, MeOH, $NaHCO_3$; (ii) HCl, MeOH.

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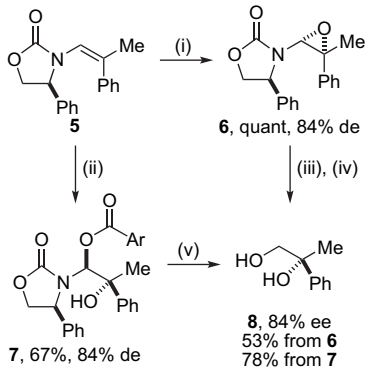
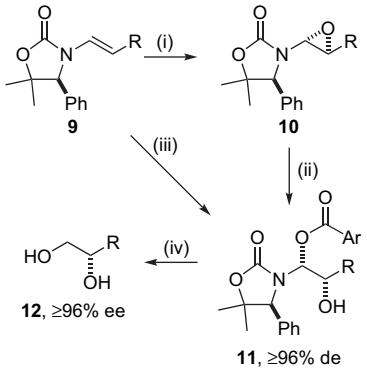
intermediate **6** in an S_N2-type process. Reduction of **7** with $NaBH_4$ gave diol **8** in 84% ee (Scheme 2).



Scheme 2. Reagents and conditions: (i) DMDO, acetone, 20 °C; (ii) *m*CBPA, $CHCl_3$, 20 °C; (iii) TsOH, acetone/H_2O (3:1), 20 °C, 30 min; (iv) $NaBH_4$, DBU, THF/H_2O (4:1), 20 °C, 15 min; (v) $NaBH_4$, EtOH, 20 °C, 24 h.

As part of our ongoing research programme for the direct synthesis of homochiral aldehydes and alcohols from *N*-acyl oxazolidinones,[8,9] through exploitation of their utility as latent aldehyde equivalents,[8] we have communicated[10] that the stereoselective epoxidation of (*E*)-enamides **9** (derived from SuperQuat 4-phenyl-5,5-dimethyl-oxazolidin-2-one) with either DMDO or *m*CPBA,[11] coupled with regio- and stereoselective S_N1-type ring opening of the intermediate epoxide **10** with *meta*-chlorobenzoic acid (*m*CBA), gave 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives **11** with excellent levels of diastereoselectivity, and suggesting that the C(1′)-configuration assigned by Adam is in error.[5b,c] Cleavage of the 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives **11** gave a range of homochiral 1,2-diols **12** with very high levels of enantiomeric purity (Scheme 3). In this manuscript, we delineate fully our investigations within this area, and report the extension of this protocol to the preparation of *O*-benzyl protected α-hydroxy ketones and esters.

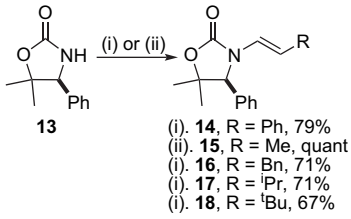


Scheme 3. Reagents and conditions: (i) DMDO, acetone, rt; (ii) *m*CBA, $CHCl_3$, rt; (iii) *m*CPBA, $CHCl_3$, rt; (iv) $NaBH_4$, MeOH, rt.

2. Results and discussion

2.1. Synthesis of SuperQuat (*E*)-enamides

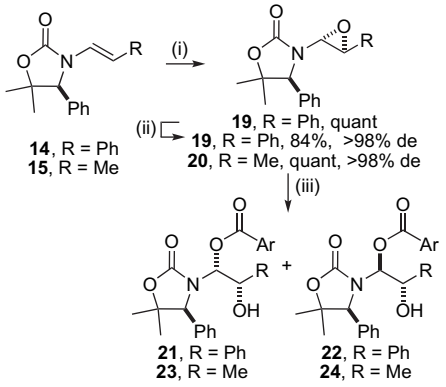
Initial investigations were concerned with the preparation of homochiral (*E*)-enamides derived from condensation of SuperQuat (*S*)-4-phenyl-5,5-dimethyl-oxazolidin-2-one[12] **13** with an aldehyde. Treatment of **13** with phenylacetaldehyde under dehydrative conditions[13] generated (*E*)-**14** as a single diastereoisomer in 79% isolated yield. Extension of this protocol to condensation of hydrocinnamaldehyde, 3-methylbutyraldehyde and 3,3-dimethylbutyraldehyde with **13** gave the corresponding (*E*)-enamides **16**–**18** as single diastereoisomers in good yield. Attempted condensation of **13** with propanal, however, furnished a complex mixture of products, presumably due to polymerisation of the aldehyde. Therefore, a copper-catalysed coupling[14] of **13** with *trans*-1-bromoprop-1-ene was employed, giving **15** in quantitative yield (Scheme 4). The configurations of enamides **14**–**18** were initially assigned on the basis of ^1H NMR spectroscopic analysis, from the diagnostic values of the olefinic coupling constants ($J_{1'-2'}$ 14.4–14.9 Hz), and in the case of **14**, **15** and **17** were subsequently proven unambiguously by single crystal X-ray analysis (vide infra).



Scheme 4. Reagents and conditions: (i) RCH_2CHO, TsOH, PhMe, Dean–Stark reflux; (ii) *trans*-1-bromoprop-1-ene, *N*,*N*′-dimethylethylenediamine, CuI, K_2CO_3, PhMe, reflux, 5 days.

2.2. Oxidation of SuperQuat (*E*)-enamides with DMDO

The epoxidation of representative SuperQuat (*E*)-enamides, viz. **14** and **15**, with DMDO was initially investigated. Oxidation of **14** (R=Ph) with an acetone solution of DMDO[15] gave epoxide **19** as the major component of a mixture of products, which precluded accurate determination of the epoxidation diastereoselectivity. However, recrystallisation of the crude reaction mixture gave **19** in 84% isolated yield and >98% de (Scheme 5).[16] Single crystal X-ray analysis unambiguously established the relative configuration of **19**, with the absolute (4*S*,1′*R*,2′*S*)-configuration assigned from the known (*S*)-stereocentre within the oxazolidinone (Fig. 1). Treatment of **15** (R=Me) with DMDO gave epoxide **20** as a single diastereoisomer, the configuration of which was assigned by analogy to that of **19** (Scheme 5). The regioselectivity of ring opening of epoxides **19** and **20** upon treatment with *m*CBA was next established. Addition of *m*CBA to either the crude or the isolated epoxide **19** (>98% de) resulted, in both cases, in the quantitative formation of a 96:4 mixture of the *C*(1′)-epimeric 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives **21** and **22**, respectively (Scheme 5). The



Enamide	R	Conditions	Products	dr[a] %
14	Ph	(i) - (iii)	**21**:**22**	96:4
14	Ph	(i) then (iii)	**21**:**22**	96:4
15	Me	(i) then (iii)	**23**:**24**	>99:<1

Scheme 5. Reagents and conditions: (i) DMDO, acetone, 0 °C to rt, 1 h; (ii) recrystallisation; (iii) *m*CBA, $CHCl_3$, 0 °C to rt, 3 h. [[a]Crude product ratio of 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives **21**/**22** or **23**/**24**; Ar=*m*-ClC_6H_4.]

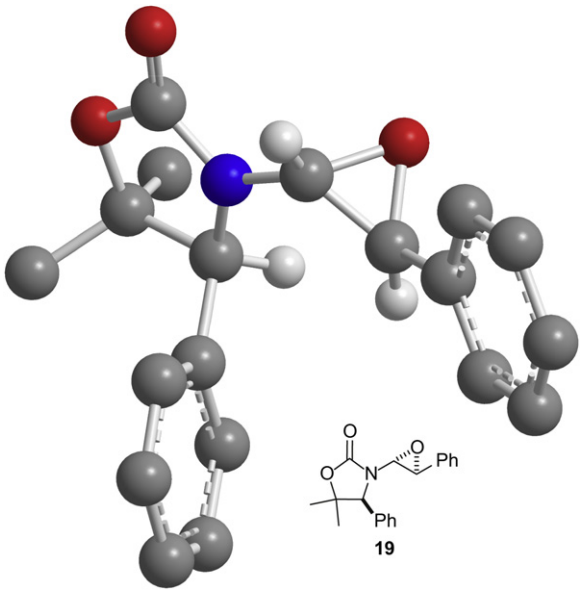


Figure 1. Chem 3D representation of the X-ray crystal structure of **19** (some H atoms removed for clarity).

observation of identical product distributions from ring opening of either the crude or the purified (>98% de) epoxide is consistent with **19** being formed as a single diastereoisomer in the oxidation with DMDO. The relative configuration within the major product **21** resulting from epoxide opening was unambiguously established by single crystal X-ray analysis,[17] with the absolute (4*S*,1′*R*,2′*S*)-configuration being assigned from the known (*S*)-stereocentre of the oxazolidinone. The assignment of the minor product **22** as a diastereoisomer (rather than regioisomer) of **21** was made on the basis of ^{1}H NMR analysis, which revealed signals at δ_H 6.24 and 6.07 ppm for C(1′)*H*, and at δ_H 5.66 and 5.65 ppm for C(2′)*H* of **21** and **22**, respectively, characteristic of the *m*-chlorobenzoyl substituent being present at C(1′), and consistent with observations made by Hsung[5a] and Adam.[5b,c] Epoxide opening of **20** (R=Me) with *m*CBA gave **23** in >98% de quantitatively (Scheme 5). The relative configuration within **23** was unambiguously established by single crystal X-ray analysis, with the absolute (4*S*,1′*R*,2′*S*)-configuration being assigned from the known (*S*)-stereocentre of the oxazolidinone (Fig. 2).

The observed *syn*-selectivity in these epoxide opening reactions is in contrast to the *anti*-selectivity assumed by Adam et al. upon

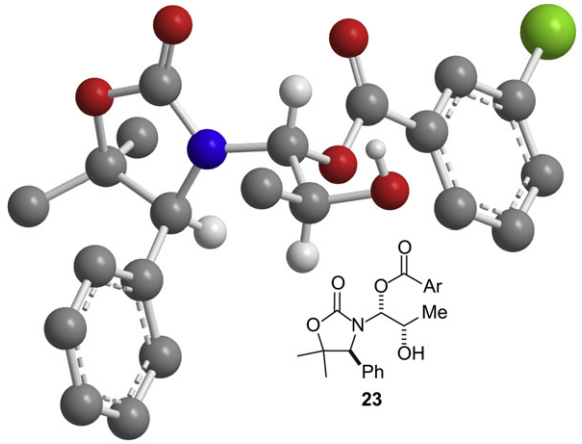


Figure 2. Chem 3D representation of the X-ray crystal structure of **23** (some H atoms removed for clarity) [Ar=*m*-ClC$_6$H$_4$].

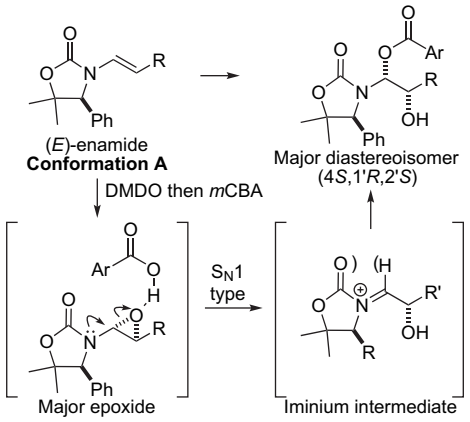
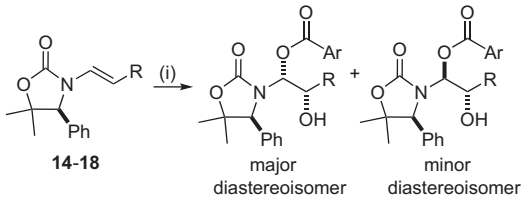


Figure 3. Postulated mechanism for oxidation of SuperQuat (*E*)-enamides [Ar=*m*-ClC$_6$H$_4$].

analogous oxidation of Evans oxazolidinone enamides,[5b,c] and furthermore is inconsistent with a mechanism involving regioselective S_N2-type opening of the epoxide.[18] The alternative mechanism involving epoxide opening in an S_N1-type process to give an *N*-acyl iminium intermediate, which is trapped stereoselectively by *m*-chlorobenzoate is consistent with the data herein. The selectivity in this oxidation protocol therefore arises as a result of two distinct mechanistic steps: enamide oxidation installs the C(2′)-stereocentre whilst the selectivity of the iminium trap by *m*CBA installs the C(1′)-stereocentre. The stereochemistry within epoxides **19** and **20** is consistent with oxidation occurring with high diastereoselectivity *anti* to the stereodirecting group of the oxazolidinone with the enamide in conformation **A**. The subsequent selectivity observed upon trapping of the corresponding iminium intermediate may be under the control of the oxazolidinone, with addition of *m*CBA occurring *anti* to the stereodirecting group, although hydrogen-bonded delivery by the *C*(2′)-hydroxyl group may also be involved (Fig. 3).

2.3. Oxidation of SuperQuat (*E*)-enamides with *m*CPBA

Investigations next turned to assessment of the reactivity of the enamide functionality towards oxidation with *m*CPBA, in order to prepare the 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives in one step. Thus, oxidation of enamide **14** (R=Ph) with *m*CPBA proceeded to give a 96:4 mixture of the *C*(1′)-epimers **21**/**22** (i.e., with identical selectivity to that observed upon sequential treatment with DMDO then *m*CBA). Recrystallisation of the crude reaction mixture gave **21** in >98% de and 84% isolated yield. Analogous oxidation of enamide **15** (R=Me) also proceeded with identical levels of selectivity as the two-step process, giving **23** as a single diastereoisomer (dr >99:<1, **23**/**24**), which was isolated in 95% yield after recrystallisation. Application to the range of (*E*)-enamides **16**–**18** was next investigated and proceeded, in each case, with excellent levels of diastereoselectivity to give the corresponding (4*S*,1′*R*,2′*S*)-1′-*m*-chlorobenzoyl-2′-hydroxy derivatives **25**, **27** and **29** as the major diastereoisomeric products. Recrystallisation of the crude reaction mixture allowed the isolation of **25** and **27** as single diastereoisomers, although **29** was not amenable to recrystallisation and proved extremely labile, fragmenting to a complex mixture of products upon attempted purification by chromatography, and was therefore characterised from the crude reaction mixture (Scheme 6). The relative configuration within **25** (R=Bn) was unambiguously established by single crystal X-ray analysis, with the absolute (4*S*,1′*R*,2′*S*)-configuration assigned from the known (*S*)-stereocentre within the oxazolidinone (Fig. 4). The



Enamide	R	Products	dr[a]	Yield (de) %[b]
14	Ph	21:22	96:4	84 (>98)
15	Me	23:24	>99:<1	95 (>98)
16	Bn	25:26	96:4	60 (>98)
17	^{i}Pr	27:28	96:4	61 (>98)
18	^{t}Bu	29:30	98:2	quant (96)[a]

Scheme 6. Reagents and conditions: (i) *m*CPBA, $CHCl_3$, 0 °C to rt, 2.5 h. [[a]Crude product ratio; [b] purified—isolated yield and de of major diastereoisomer; Ar=*m*-ClC_6H_4.]

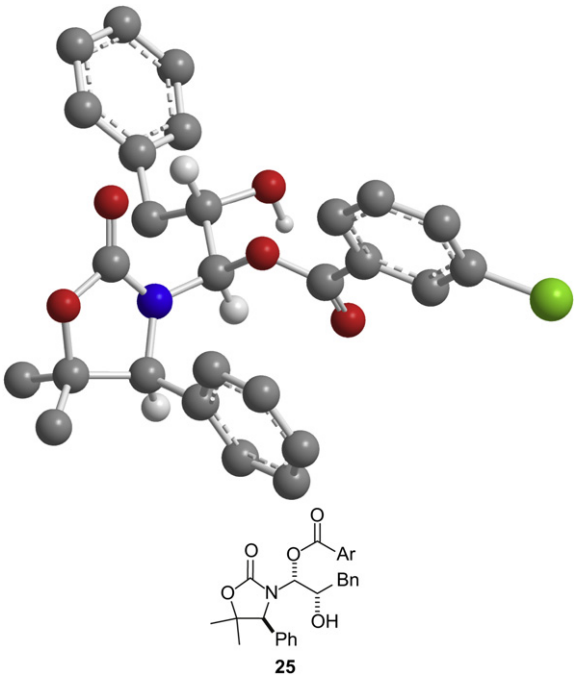


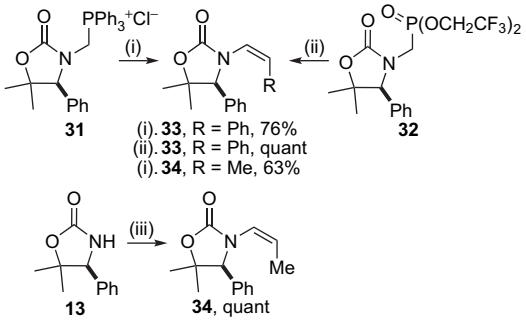
Figure 4. Chem 3D representation of the X-ray crystal structure of **25** (some H atoms removed for clarity) [Ar=*m*-ClC_6H_4].

(4*S*,1′*R*,2′*S*)-configurations of major diastereoisomers **27** (R=^{i}Pr) and **29** (R=^{t}Bu) were assigned by analogy to those unambiguously established for **21**, **23** and **25**. These observations are entirely consistent with the oxidation with *m*CPBA proceeding via the intermediacy of the corresponding diastereoisomerically pure epoxide.

The effect of changing the geometry of the enamide system from (*E*) to (*Z*) upon the diastereoselectivity of these processes was next examined by the preparation and subsequent oxidation of SuperQuat (*Z*)-enamides.

2.4. Synthesis of SuperQuat (*Z*)-enamides

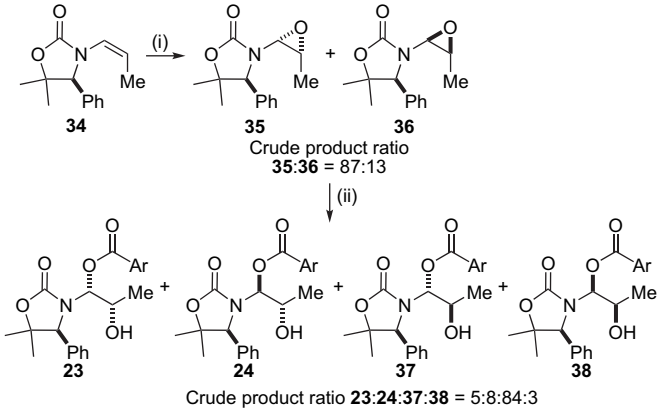
In order to access SuperQuat (*Z*)-enamides, olefination of benzaldehyde and acetaldehyde with the ylide derived from the novel precursor **31**[19] gave 9:91 and 20:80 (*E*)/(*Z*) mixtures, respectively, from which (*Z*)-enamides **33** and **34** were isolated as single diastereoisomers in 76 and 63% yield, respectively.[20] In order to improve both the selectivity and the yield of enamide formation, olefination of benzaldehyde with the novel phosphonate ester **32** according to the Still–Gennari protocol[21] was investigated and furnished exclusively **33**, in quantitative yield after chromatographic purification. Reaction of **32** with acetaldehyde generated a complex mixture of unidentifiable products and therefore copper-catalysed coupling[14] of SuperQuat **13** with *cis*-1-bromoprop-1-ene was utilised, which gave **34** in quantitative yield (Scheme 7). The configurations of enamides **33** and **34** were initially assigned on the basis of the diagnostic olefinic coupling constants ($J_{1'-2'}$ 7.1–9.6 Hz) and were subsequently proven unambiguously by single crystal X-ray analysis (vide infra).



Scheme 7. Reagents and conditions: (i) KO^{t}Bu, THF, −78 °C, 30 min, then RCHO, −78 °C, 24 h; (ii) BuLi, THF, −78 °C, 30 min, then PhCHO, −78 °C, 24 h; (iii) *cis*-1-bromoprop-1-ene, *N*,*N*′-dimethylethylenediamine, CuI, K_2CO_3, PhMe, reflux, 5 days.

2.5. Oxidation of SuperQuat (*Z*)-enamides with DMDO

Investigations into the oxidation of (*Z*)-enamides with DMDO revealed that treatment of **34** (R=Me) with DMDO gave an 87:13 mixture (74% de) of diastereoisomeric epoxides **35**/**36**. Subsequent epoxide opening upon treatment with *m*CBA furnished a 5:8:84:3 mixture of diastereoisomers **23**/**24**/**37**/**38** (Scheme 8). The relative stereochemistry within the major diastereoisomer **37** was unambiguously established by single crystal X-ray analysis, with the absolute (4*S*,1′*R*,2′*R*)-configuration assigned from the known (*S*)-stereocentre within the oxazolidinone (Fig. 5). Since the diastereoisomeric ratio of the epoxide also represents the diastereoisomeric ratio at the C(2′)-stereocentre within the 1′-*m*-chlorobenzoyl-2′-hydroxy oxidation products, and the absolute configurations of **23** and **37** had been unambiguously assigned via single crystal X-ray analysis, the absolute configurations of minor diastereoisomers **24** and **38** could thus be assigned, i.e., [**23**+**24**]/[**37**+**38**]=13:87 (Scheme 8).



Scheme 8. Reagents and conditions: (i) DMDO, acetone, 0 °C to rt, 1 h; (ii) *m*CBA, $CHCl_3$, 0 °C to rt, 3 h. [[a]Crude product ratio; Ar=*m*-ClC_6H_4.]

Treatment of **33** (R=Ph) with DMDO gave a mixture of products, the two major components of which were identified as the epoxide **39** and diol **40** in a 93:7 ratio (Scheme 9). A minor diastereoisomeric

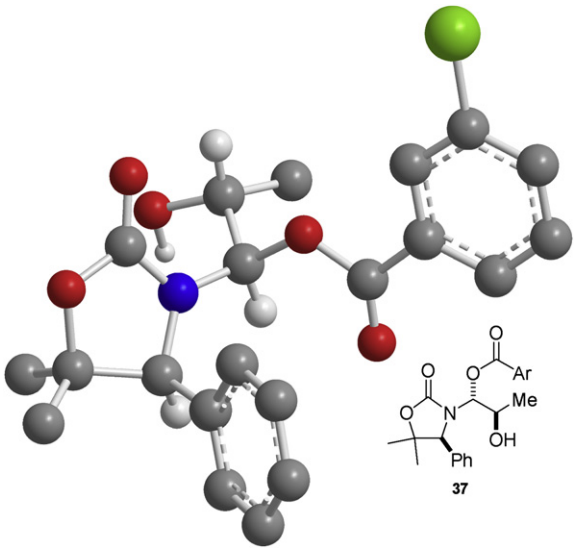


Figure 5. Chem 3D representation of the X-ray crystal structure of **37** (some H atoms removed for clarity) [Ar=*m*-ClC_6H_4].

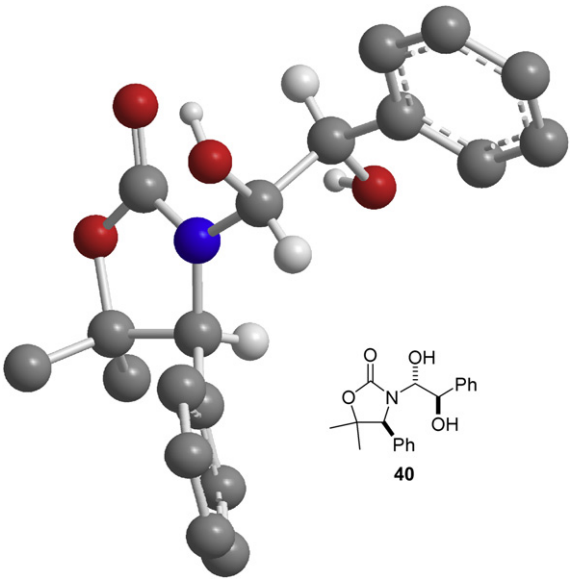
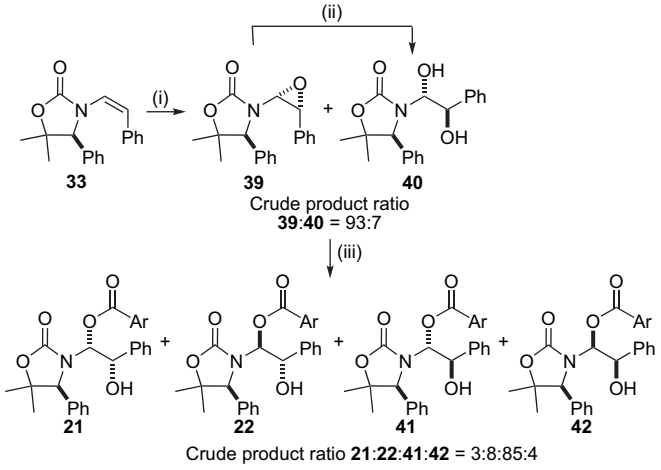


Figure 6. Chem 3D representation of the X-ray crystal structure of **40** (some H atoms removed for clarity).



Scheme 9. Reagents and conditions: (i) DMDO, acetone, 0 °C to rt, 1 h; (ii) recrystallisation; (iii) *m*CBA, $CHCl_3$, 0 °C to rt, 3 h. [[a]Crude product ratio; Ar=*m*-ClC_6H_4.]

epoxide could not be unambiguously identified in the ^{1}H NMR spectrum of the crude reaction mixture, precluding an assessment of the epoxide diastereoisomeric ratio. Attempted recrystallisation of the crude reaction mixture furnished diol **40** only. Single crystal X-ray analysis unambiguously established the relative configuration of **40**, with the absolute (4*S*,1′*R*,2′*R*)-configuration assigned from the known (*S*)-stereocentre of the oxazolidinone (Fig. 6). This unambiguously confirmed the (2′*R*)-configuration, and corroborates the (4*S*,1′*R*,2′*R*)-configuration, of the major epoxide **39**. The observed stereochemistry within diol **40** is in accordance with **40** arising from stereoselective S_N1-type ring opening of epoxide **39** by adventitious water. Treatment of the crude mixture of **39** and **40** with *m*CBA gave a 3:8:85:4 mixture of **21**/**22**/**41**/**42** (Scheme 9). Diastereoisomers **21** and **22** were spectroscopically identical to the products resulting from oxidation of the corresponding (*E*)-enamide **14**. The absolute configuration of the major diastereoisomeric product **41** in this protocol was assigned by direct analogy to that unambiguously proven for **37** (R=Me). Therefore, the configuration within the remaining diastereoisomer (4*S*,1′*S*,2′*R*)-**42** could be assigned. Given that the diastereoisomeric ratio at the C(2′)-stereocentre within the 1′-*m*-chlorobenzoyl-2′-hydroxy oxidation products also represents the epoxide diastereoisomeric ratio, this can be inferred as 89:11 (78% de), i.e., [**21**+**22**]/[**41**+**42**]=11:89.

Thus, whilst oxidation of (*E*)-enamides **14** and **15** gives (4*S*,1′*R*,2′*S*)-**21** and (4*S*,1′*R*,2′*S*)-**23** as the major products, oxidation of the corresponding (*Z*)-enamides **33** and **34** gives (4*S*,1′*R*,2′*R*)-**41** and (4*S*,1′*R*,2′*R*)-**37** as the major products, with the *opposite* configuration at C(2′) but the *same* configuration at C(1′), which is entirely consistent with our mechanistic rationale involving stereoselective S_N1-type ring opening of the epoxide intermediate (Fig. 7).

2.6. Oxidation of SuperQuat (*Z*)-enamides with *m*CPBA

Oxidation of **33** (R=Ph) with *m*CPBA gave a 5:14:77:4 mixture of diastereoisomers **21**/**22**/**41**/**42**, respectively, from which the major diastereoisomer **41** was isolated in 57% yield and >98% de after recrystallisation. Oxidation of **34** (R=Me) with *m*CPBA gave a 7:10:81:2 mixture of **23**/**24**/**37**/**38** from which the major product **37** was isolated in >98% de and 41% yield after recrystallisation (Scheme 10). In both cases, the product distribution is consistent with that seen in the two-step (DMDO then *m*CBA) process and is

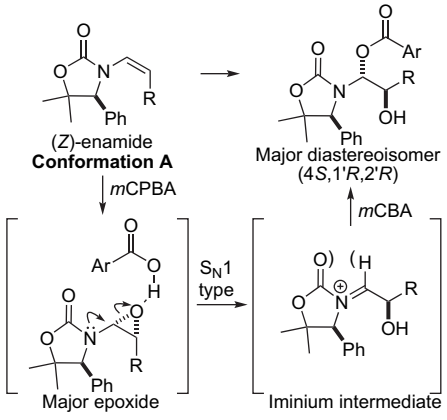
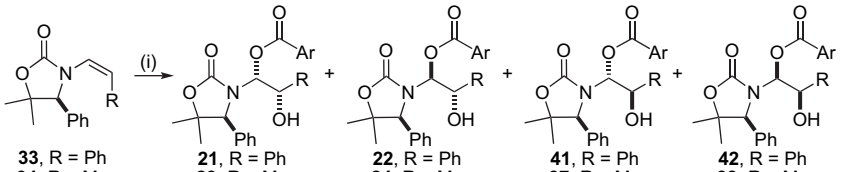


Figure 7. Postulated mechanism for oxidation of SuperQuat (*Z*)-enamides [Ar=*m*-ClC_6H_4].



Enamide	R	Products	dr[a]	Yield (de) %[b]
33	Ph	21:22:41:42	5:14:77:4	57 (>98)
34	Me	23:24:37:38	7:10:81:2	41 (>98)

Scheme 10. Reagents and conditions: (i) *m*CPBA, $CHCl_3$, 0 °C to rt, 2.5 h. [[a]Crude product ratio; [b]purified—isolated yield and de of major diastereoisomer; Ar=*m*-ClC_6H_4.]

consistent with the reaction proceeding via the corresponding epoxide intermediate.

2.7. Solid and solution-phase conformations of SuperQuat enamides

In order to probe the origin of the lower levels of selectivity observed upon the oxidative functionalisation of (*Z*)-enamides **33** and **34** as compared to their (*E*)-counterparts **14** and **15**, respectively, their preferred conformations were investigated. Single crystal X-ray analysis of **14**, **15**, **33** and **34** confirmed the assigned enamide configurations and allowed the solid state conformations to be probed (Fig 8). For (*E*)-enamides **14** and **15**, the enamide system lies approximately planar as indicated by the values of the dihedral angles *C*(2)–*N*(3)–*C*(1′)–C(1′)*H* (φ_1), and *N*(3)–*C*(1′)–*C*(2′)–C(2′)*H* for (*E*)-enamides, or *N*(3)–*C*(1′)–*C*(2′)–C(2′)*R* for (*Z*)-enamides (φ_2). For (*Z*)-enamides **33** and **34**, significant deviation from planarity is noted and is presumably the result of unfavourable steric interactions between the *C*(2′)-substituent and the oxazolidinone framework. For all enamides **14**, **15**, **33** and **34**, however, *s-trans* conformation **A** is preferred over *s-cis* conformation **B** to minimise steric interactions between the enamide system and the oxazolidinone carbonyl group (Fig. 9). Similar solution-phase enamide conformations were inferred from UV studies: λ_{max} for **33** and **34** is shifted to lower wavelengths as compared to the corresponding (*E*)-enamides **14** and **15**, with a concomitant reduction in the value of the molar extinction coefficient. These effects are more pronounced in the β-styryl-enamides: for **14**, λ_{max} 275.11 nm, ε=27103×10^3 cm^2 mol^{-1}, cf. **33**, λ_{max} 259.45 nm, ε=14864×10^3 cm^2 mol^{-1}; for **15** λ_{max} 240.65 nm, ε=2661×10^3 cm^2 mol^{-1}, cf.

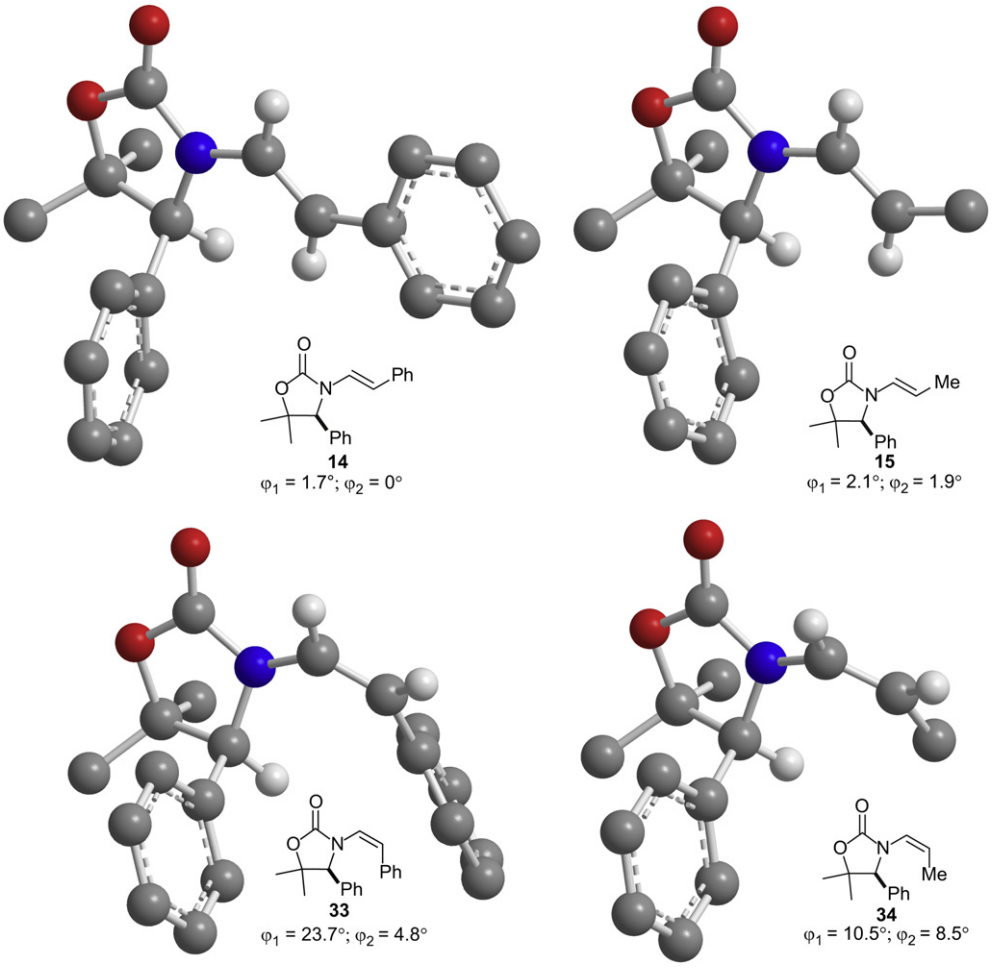
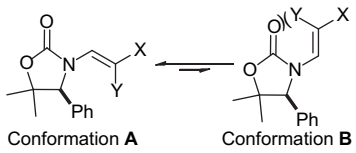


Figure 8. Chem 3D representations of the single crystal X-ray structures of **14**, **15**, **33** and **34** (some H atoms removed for clarity).



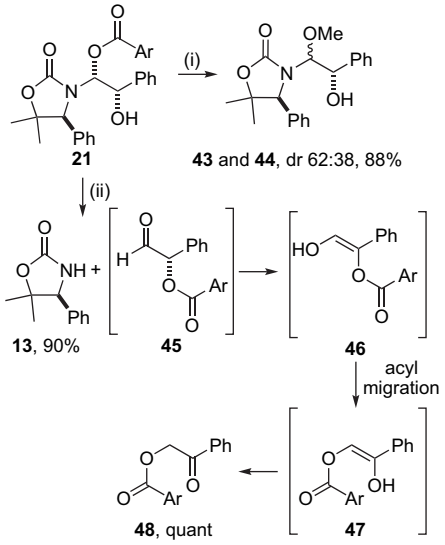
Enamide	X,Y	λ_{max} nm	ε	$10^3 cm^2 mol^{-1}$
14	X = Ph,Y = H	275.11		27103
15	X = Me,Y = H	240.65		2661
33	X = H,Y = Ph	259.45		14864
34	X = H,Y = Me	240.06		1944

Figure 9. UV data and conformations of SuperQuat enamides.

34, λ_{max} 240.06 nm, ε=1944×10^3 cm^2 mol^{-1} (Fig. 9). These results are therefore suggestive that, as a result of the distortion from planarity of the enamide system, the *C*(4)-phenyl stereodirecting group is less well able to shield one face of the (*Z*)-enamide when compared to the corresponding (*E*)-enamide, resulting in a lowering of the diastereofacial selectivity upon epoxidation, which is consistent with our experimental observations.

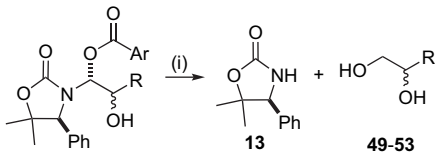
2.8. Synthesis of homochiral 1,2-diols

With single diastereoisomers of 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives available, their hydrolysis to furnish α-hydroxy aldehydes was investigated. It is known that α-hydroxy aldehydes readily undergo dimerisation[22] or rearrangement to α-hydroxy ketones,[23] and are therefore usually obtained in protected forms.[24] Unfortunately, attempted methanolysis of **21** gave a 62:38 mixture of diastereoisomeric α-methoxy compounds **43**/**44**, which was stable even upon prolonged heating, whilst all attempts to protect the hydroxyl group of **21** (to facilitate subsequent acidic hydrolysis)[8] gave a complex mixture of products, of which SuperQuat **13** and ketone **48** were the only identifiable components; treatment of **21** with Et_3N and DMAP gave **13** and **48** as the only products. This may be explained by decomposition of **21** via acyl transfer to the *C*(2′)-hydroxyl group followed by cleavage to SuperQuat **13** and α-hydroxyaldehyde **45**, which subsequently isomerises under the basic reaction conditions[25] to give **48** (Scheme 11).



Scheme 11. Reagents and conditions: (i) MeOH, TsOH, reflux; (ii) Et_3N, DMAP [Ar=*m*-ClC_6H_4].

Following the recalcitrance of **21** towards hydrolysis, reduction to the corresponding homochiral 1,2-diol was investigated. Treatment of (4*S*,1′*R*,2′*S*)-**21** with $NaBH_4$ in MeOH furnished (*S*)-1-phenylethane-1,2-diol (*S*)-**49**, which, after separation from the SuperQuat auxiliary **13** by chromatography, was isolated in 81% yield and >98% ee {$[\alpha]_D^{22}$ +64.0 (*c* 0.25, $CHCl_3$); lit.[26] $[\alpha]_D^{20}$ +60.5 (*c* 1.15, $CHCl_3$)}. Analogous treatment of (4*S*,1′*R*,2′*R*)-**41** gave (*R*)-1-phenylethane-1,2-diol (*R*)-**49** in 60% yield and >98% ee {$[\alpha]_D^{19}$ −54.1 (*c* 0.9, $CHCl_3$)}. Reduction of (4*S*,1′*R*,2′*S*)-**23** with $NaBH_4$ allowed the isolation of (*S*)-propane-1,2-diol (*S*)-**50** in 37% yield and >98% ee after distillation {$[\alpha]_D^{23}$ +18.1 (*c* 0.15, H_2O); lit.[27] $[\alpha]_D^{31}$ +20.7 (*c* 7.5, H_2O)}. Similarly, reduction of (4*S*,1′*R*,2′*R*)-**37** gave (*R*)-propane-1,2-diol (*R*)-**50** in 40% yield and >98% ee {$[\alpha]_D^{23}$ −19.6 (*c* 1.6, H_2O)}. Meanwhile, reduction of **25** (>98% de) with $NaBH_4$ gave (*S*)-3-phenylpropane-1,2-diol (*S*)-**51** {$[\alpha]_D^{24}$ −33.5 (*c* 0.9, EtOH), lit.[28] $[\alpha]_D^{20}$ −36 (*c* 1.0, EtOH)} in 93% yield and >98% ee. Although similar reduction of **27** (>98% de) with $NaBH_4$ led to low isolated yields of the corresponding diol, treatment with $LiAlH_4$ allowed the direct isolation of diol (*S*)-**52** in 56% yield and in 96% ee. Application of this reduction protocol to a freshly prepared sample of crude enamide **29** (96% de) with $LiAlH_4$ allowed the isolation of diol (*S*)-**53** in 51% yield and 96% ee (Scheme 12).



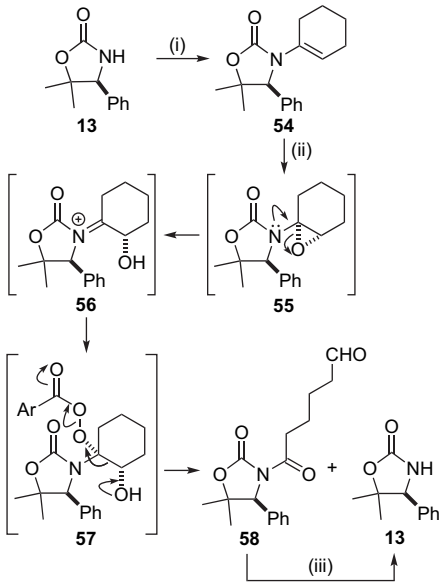
	R	Yield 13 %	Diol	Yield diol %	ee %[a]
(4*S*,1′*R*,2′*S*)-**21**	Ph	78	(*S*)-**49**	81	>98
(4*S*,1′*R*,2′*R*)-**41**	Ph	90	(*R*)-**49**	60	>98
(4*S*,1′*R*,2′*S*)-**23**	Me	99	(*S*)-**50**	37	>98
(4*S*,1′*R*,2′*R*)-**37**	Me	90	(*R*)-**50**	40	>98
(4*S*,1′*R*,2′*S*)-**25**	Bn	99	(*S*)-**51**	93	>98
(4*S*,1′*R*,2′*S*)-**27**	^{i}Pr	81	(*S*)-**52**	56	96
(4*S*,1′*R*,2′*S*)-**29**	^{t}Bu	84	(*S*)-**53**	51	96

Scheme 12. Reagents and conditions: (i) $NaBH_4$, MeOH, rt; (ii) $LiAlH_4$, THF, rt. [[a]Enantiomeric excess values were determined by chiral GC analysis of diol **49**, the diacetyl derivatives of diols **50**, **52** and **53**, and the bis-trifluoroacetyl derivative of **51**; Ar=*m*-ClC_6H_4.]

2.9. Oxidative functionalisation of SuperQuat enamides derived from a ketone

Following the successful application of this enamide oxidation protocol to the synthesis of 1,2-diols, extension to incorporate the synthesis of α-hydroxy ketones was examined. Initial studies probed the oxidation of cyclohexenyl enamide **54**, derived from condensation of SuperQuat **13** with cyclohexanone. Treatment of **54** with *m*CPBA gave a 78:22 mixture of SuperQuat **13** and aldehyde **58**. Repetition of this protocol omitting aqueous work-up gave predominantly **58** (>90%), although attempted purification of the crude reaction mixture returned only SuperQuat **13**. These results suggest that epoxidation was occurring, followed by ring opening and trapping of the resultant *N*-acyl iminium intermediate **56** by *m*CPBA to generate **57**.[29] Collapse of **57** liberates aldehyde **58**, which upon hydrolysis regenerates SuperQuat **13**. Although this oxidation pathway contrasts with the oxidation of the aldehyde derived systems, a plausible rationale for the addition of *m*CPBA to the cyclohexenyl system may be due to the greater inductive stability of the ketone derived *N*-acyl iminium intermediate as compared to the aldehyde derived system (Scheme 13).

To address the problem of oxidative ring cleavage, it was envisaged that epoxidation in a nucleophilic alcohol solvent such as methanol may suppress the unwanted fragmentation by competitive trapping of the *N*-acyl iminium intermediate **56**. Treatment of **54** with *m*CPBA in anhydrous MeOH at 0 °C gave a 66:30:3:1 ratio of **59**/**60**/**61**/**62**. The effect of temperature on the diastereoselectivity was next investigated, with the optimum conversion



Scheme 13. Reagents and conditions: (i) cyclohexanone, TsOH, PhMe, Dean–Stark reflux; (ii) *m*CPBA, DCM, 0 °C, molecular sieves, 12 h; (iii) chromatography on SiO_2.

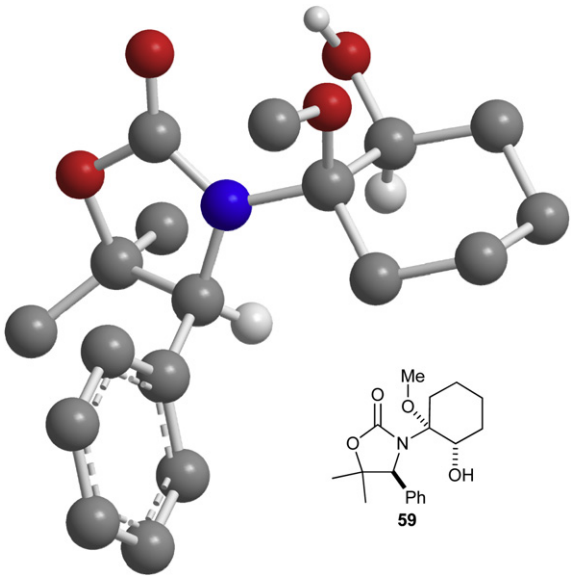


Figure 10. Chem 3D representation of the X-ray crystal structure of **59** (some H atoms removed for clarity).

and diastereocontrol observed at −20 °C, giving a 67:30:2:1 ratio of **59**/**60**/**61**/**62**; subsequent chromatography gave **59**, **60** and **61** in 50, 26 and (higher than expected) 11% yield, respectively, and in >98% de in each case (Scheme 14).

The relative configurations within **59**–**61** were determined from ^{1}H NMR NOESY experiments, with those of **59** and **61** being confirmed unambiguously by single crystal X-ray analysis (Figs. 10 and 11). The absolute configurations (4*S*,1′*R*,2′*S*)-**59**, (4*S*,1′*S*,2′*R*)-**60** and (4*S*,1′*S*,2′*S*)-**61** were thus assigned from the known (*S*)-stereocentre within the oxazolidinone.

The isolated yield of **61** (11%) was significantly higher than the proportion indicated by analysis of the crude reaction mixture, and most likely originates from interconversion of **59** and **61** during chromatography. In support of this hypothesis, a pure sample of **59** (>98% de) was treated with a catalytic amount of sulfuric acid in MeOH-d_4, and the reaction was monitored over time by ^{1}H NMR spectroscopy: complete epimerisation of **59**-d_3 to **61**-d_3 (>98% de) was observed, demonstrating that **61** is the thermodynamically more stable isomer (Scheme 15). These results are in accordance with observations made by Zefirov et al. in studies on 1,1,2-trisubstituted cyclohexanes in which the 2-substituent preferentially lies axial due to minimisation of *syn*-pentane interactions.[30]

In contrast to the high diastereocontrol observed in the oxidative functionalisation of aldehyde derived SuperQuat enamides, only modest stereoselectivity is seen in the cyclohexenyl system. The selectivity in the oxidation of the cyclohexenyl system is assumed to be controlled by similar factors to the aldehyde derived enamide system, with the oxidation occurring *anti* to the phenyl

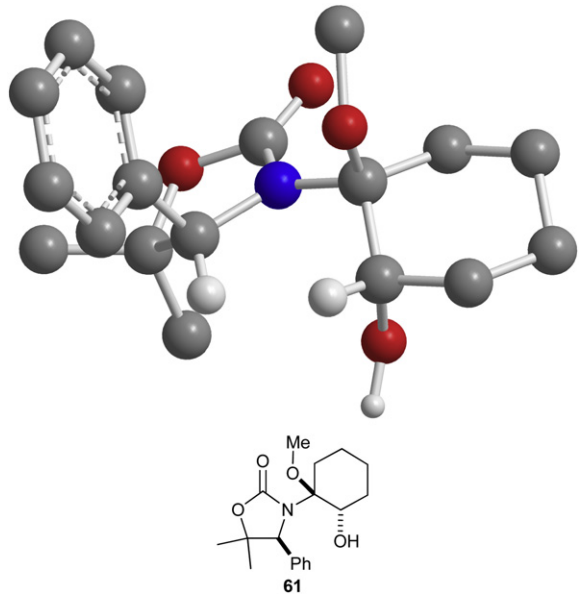
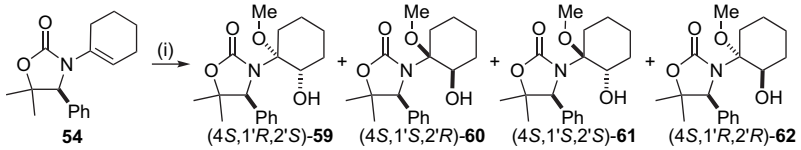


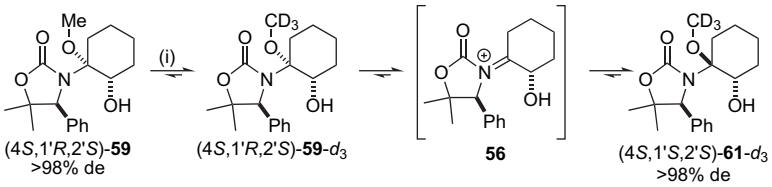
Figure 11. Chem 3D representation of the X-ray crystal structure of **61** (some H atoms removed for clarity).

substituent on the oxazolidinone ring. The selectivity of the epoxidation is represented by the ratio of the (*S*) to (*R*) configurations at the C(2′) position; hence, under the optimum reaction conditions,



Temperature °C	Time h	Conversion %	Ratio 59:60:61:62
−40	2	35	80:17:2:1
−20	2	100	67:30:2:1
0	1	100	66:30:3:1
20	1	100	64:30:5:1

Scheme 14. Reagents and conditions: (i) *m*CPBA, MeOH, *T* °C, *X* h (see table).



Scheme 15. Reagents and conditions: (i) MeOH-d_4, H_2SO_4 (cat).

the epoxide diastereoisomeric ratio is 69:31 ([**59**+**61**]/[**60**+**62**]). Stereoselective oxidation of **54** in conformation **C**, *anti* to the stereodirecting group of the oxazolidinone generates epoxide **55** from which **59** and **61** are subsequently derived. Diastereoisomers **60** and **62** originate from either non-stereoselective epoxidation of **54** in conformation **C** or stereoselective epoxidation of **54** in conformation **D**, followed by regioselective epoxide opening by MeOH, although single crystal X-ray analysis of **54** indicates that in the solid state the cyclohexene ring exclusively adopts conformation **C**, which places the enamide double bond in the plane of the oxazolidinone ring system with the methylene group straddling the carbonyl group to minimise steric interactions (Fig. 12). The 67:2 ratio of *C*(1′) epimers **59** and **61**, and 30:1 ratio of *C*(1′) epimers **60** and **62** show that the trapping of the corresponding *N*-acyl iminium intermediates by MeOH (under kinetic control) occurs with high *syn*-selectivity with respect to the *C*(2′)-hydroxyl group for both epoxide diastereoisomers (Fig. 13).

The hydrolytic cleavage of **59** and **61** to α-hydroxycyclohexanone **63** was next examined. Treatment of **59** with HCl in THF gave a mixture of **63** and SuperQuat **13**, from which **63** was isolated by chromatography in 55% yield (Scheme 16). The specific rotation of **63** was considerably lower than the literature values {$[\alpha]_D^{20}$ −1.5 (*c* 1.0, $CHCl_3$); lit.[31] for 90% ee $[\alpha]_D^{20}$ −13.3 (*c* 0.5, $CHCl_3$); lit.[32] for enantiomer, 96% ee $[\alpha]_D^{18}$ +23.3 (*c* 0.6, $CHCl_3$)}, suggesting that extensive racemisation had occurred[33] and therefore protection of the hydroxyl group prior to hydrolysis was probed. Benzylation of (4*S*,1′*R*,2′*S*)-**59** was followed by chromatography, giving (*S*)-α-benzyloxycyclohexanone (*S*)-**66** in 9% yield and indicating that **64** is unstable towards hydrolysis. Benzylation of the thermodynamically more stable diastereoisomer (4*S*,1′*S*,2′*S*)-**61** gave **65** in 95% isolated yield with subsequent hydrolysis giving (*S*)-**66** in 69% yield {$[\alpha]_D^{23}$ −103.0 (*c* 0.8, $CHCl_3$); lit.[34] $[\alpha]_D^{21}$ −108.1 (*c* 1.2, $CHCl_3$)} (Scheme 16).

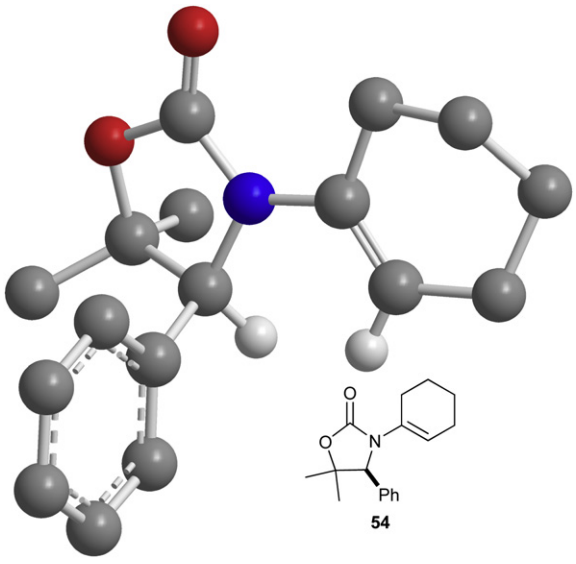


Figure 12. Chem 3D representation of the X-ray crystal structure of **54** (some H atoms removed for clarity).

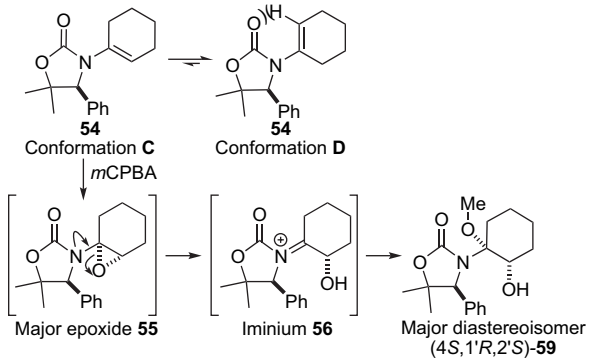
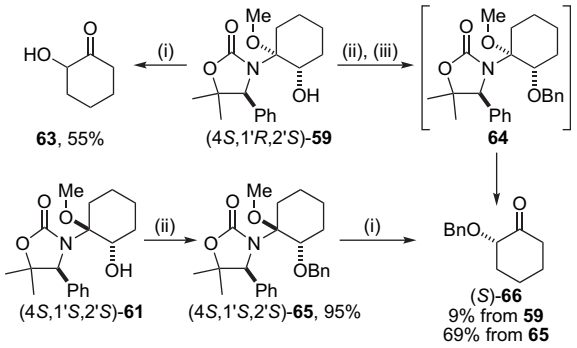


Figure 13. Postulated mechanism for oxidation of enamide **54**.



Scheme 16. Reagents and conditions: (i) HCl (10% aq), THF, 2 h; (ii) NaH, BnBr, DMF; (iii) chromatography on SiO_2.

2.10. Stereoselective functionalisation of SuperQuat enamides via C(1′)-lithiation

In order to extend the utility of this methodology for the synthesis of α-hydroxy carbonyl compounds, the ability of SuperQuat enamides to function as acyl anion equivalents through lithiation, subsequent reaction with an aldehyde, and hydrolysis was investigated. It was anticipated that regioselective lithiation of SuperQuat enamides **67** followed by stereoselective aldol reaction[35] would generate α-substituted enamides **69** that would be amenable to hydrolytic cleavage to α-hydroxy ketones **70**, or oxidative C=C cleavage followed by alcoholysis to α-hydroxy esters **71** (Fig. 14).

Initial investigations focused on the functionalisation of enamides **14** and **72**,[36] which lack the capacity for γ-deprotonation.[37] Regioselective C(1′)-lithiation of **14** with ^{t}BuLi followed by addition of benzaldehyde gave a 92.5:7.5 mixture of alcohols **75** and **76** (85% de) from which the major diastereoisomer **75** was isolated in 60% yield and >98% de after sequential chromatography and recrystallisation. Meanwhile, analogous treatment of enamide **72** gave alcohols **77** and **78** as a 67:33 mixture, indicating that the presence of the (*E*)-β-phenyl group has a beneficial effect on the selectivity in this protocol. Further studies in this area therefore centred upon enamide **14** (Scheme 17).

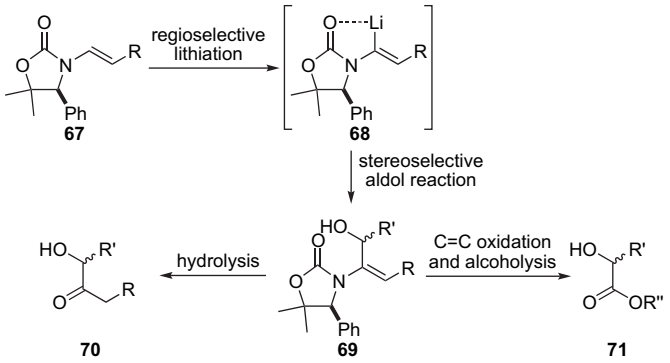
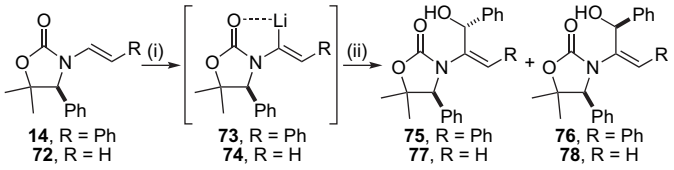


Figure 14. Proposed synthesis of α-hydroxy carbonyl compounds **70** and **71** from SuperQuat enamides **67**.



Enamide	R	Products	dr[a]	Yield (de) %[b]
14	Ph	**75**:**76**	92.5:7.5	60 (>98)
72	H	**77**:**78**	67:33	60 (34)

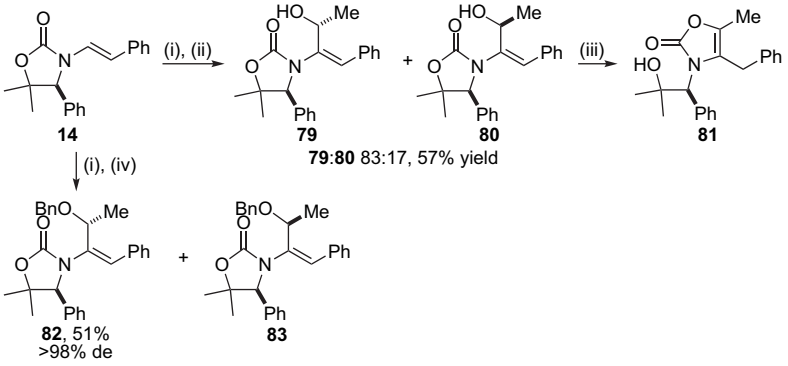
Scheme 17. Reagents and conditions: (i) ^{t}BuLi, THF, −78 °C; (ii) PhCHO. [[a]Crude product ratio; [b]purified—isolated yield and de of major diastereoisomer.]

The scope of other aldehydes that could be tolerated in the reaction protocol was next examined. Although treatment of **14** with ^{t}BuLi followed by isobutyraldehyde or pivalaldehyde furnished a complex mixture of products in both cases, with no evidence of the desired addition products, reaction with acetaldehyde gave an 83:17 mixture of **79** and **80**. Attempted separation by chromatography, however, resulted in an intramolecular rearrangement via endocyclic cleavage to afford tertiary alcohol **81** as the sole product. In order to suppress this rearrangement, an in situ *O*-benzyl protection strategy was investigated. Thus, sequential treatment of **14** with ^{t}BuLi and acetaldehyde, and subsequent addition of benzyl bromide afforded a complex mixture containing **82** and **83**. Chromatography furnished the major diastereoisomer **82** in 51% yield and >98% de (Scheme 18).

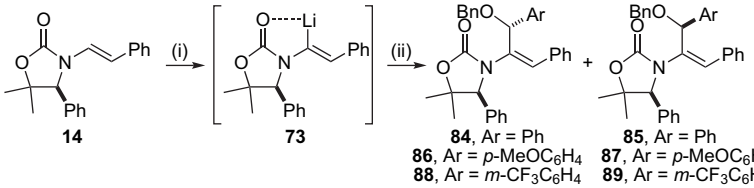
With higher levels of reactivity and diastereocontrol displayed in reaction of **14** with benzaldehyde compared to the aliphatic aldehydes, further additions to aromatic aldehydes were pursued, with in situ benzylation being preferred. Treatment of **14** with ^{t}BuLi and benzaldehyde, and subsequent addition of benzyl bromide afforded a 92:8 mixture of **84** and **85**. Purification via chromatography furnished **84** in 83% yield and >98% de. Analogous reactions employing *p*-anisaldehyde and *m*-trifluoromethylbenzaldehyde gave chromatographically separable 78:22 and 94:6 mixtures of the corresponding benzyl ethers **86**/**87** and **88**/**89**, respectively (Scheme 19).

The relative configurations within **84** and **88** were unambiguously established by single crystal X-ray analysis (Figs. 15 and 16), with the absolute (4*S*,1″*R*)-configurations assigned from the known (*S*)-stereocentre of the oxazolidinone. The absolute configurations of the other major diastereoisomers **75**, **77**, **79**, **82** and **86** were therefore assigned as (4*S*,1″*R*) by analogy.

Schmidt et al. have represented the addition of a vinyl lithium species to a carbonyl compound as a *centre–face* interaction, where the C–Li bond, *centre*, attacks the *face* of the carbonyl double bond in the aldehyde.[38] The intermediate vinyl lithium species **73** is expected to have a defined five-membered ring chelate structure due to the stabilisation of the carbanion by complexation of the lithium by the carbonyl group and whilst the origin of stereocontrol in the approach of an aldehyde to a monomeric organolithium is unclear, a simplistic model may be proposed to account for the observed stereocontrol.[38] Initial co-ordination of the aldehyde to



Scheme 18. Reagents and conditions: (i) ^{t}BuLi, THF, −78 °C; (ii) MeCHO; (iii) SiO_2; (iv) MeCHO, then BnBr.



Ar	Products	dr[a]	Yield (de) %[b]
Ph	**84**:**85**	92:8	83 (>98)
p-$MeOC_6H_4$	**86**:**87**	78:22	72 (>98)
m-$CF_3C_6H_4$	**88**:**89**	94:6	62 (>98)

Scheme 19. Reagents and conditions: (i) ^{t}BuLi, THF, −78 °C; (ii) ArCHO, then BnBr. [[a]Crude product ratio; [b]purified—isolated yield and de of major diastereoisomer.]

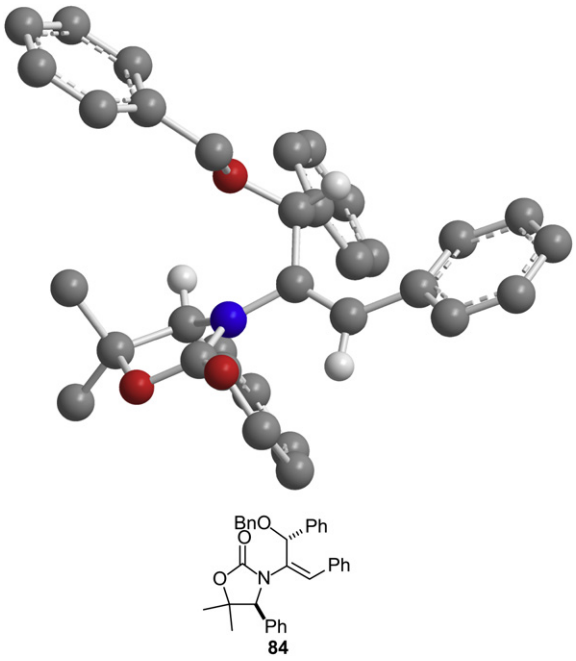


Figure 15. Chem 3D representation of the X-ray crystal structure of **84** (some H atoms removed for clarity).

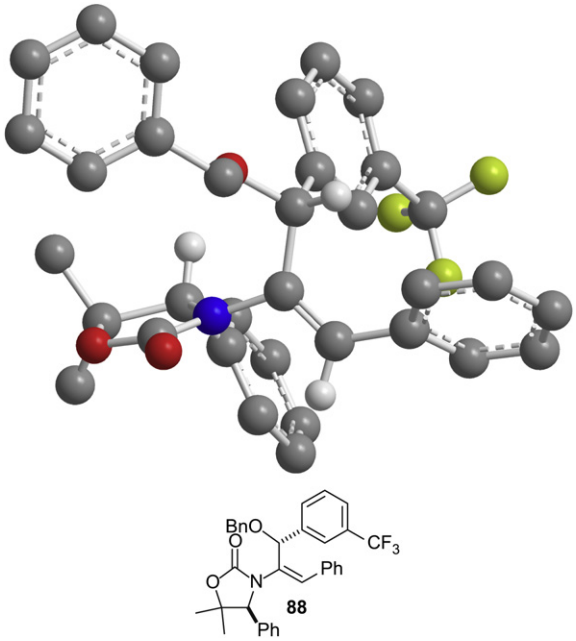


Figure 16. Chem 3D representation of the X-ray crystal structure of **88** (some H atoms removed for clarity).

the lithium atom *anti* to the stereodirecting phenyl group of the oxazolidinone and to the more sterically available lone pair of the aldehyde **90** also serves to minimise interactions between the oxazolidinone ring and the β-phenyl group of the enamide, presenting the *Si* face of the aldehyde to the enamide. Subsequent attack of the lithiated enamide on the *Si* face of the aldehyde **91** gives rise to the observed major diastereoisomer **92**. This simple model is thus able to rationalise the beneficial effect of the β-phenyl substituent in **73** (as compared to unsubstituted **74**), and the higher stereoselectivity observed on the addition to an aryl aldehyde (as compared to acetaldehyde), as potential steric interactions in these cases are likely to be more severe (Fig. 17).

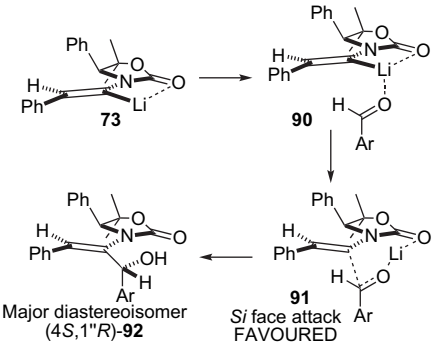
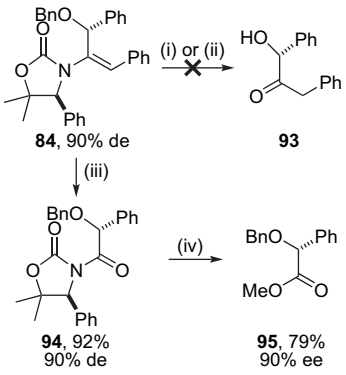


Figure 17. Plausible model for the approach of an aldehyde to lithiated enamide **73**.

The cleavage of the addition products to the corresponding α-hydroxy ketones was probed, although treatment of **84** with HCl at rt returned the starting material and subjecting **84** to similar conditions under reflux led to decomposition. Sequential C=C oxidation followed by alcoholysis of the resultant *N*-acyl oxazolidinone was therefore examined. Treatment of **84** (90% de) with sodium periodate and a catalytic amount of $RuCl_3$[39] gave the *N*-acyl product **94** in 92% isolated yield and 90% de. Methanolysis of **94** gave α-benzyloxyester **95** in 79% yield and 90% ee {$[\alpha]_D^{23}$ −84.9 (*c* 1.15, $CHCl_3$); lit.[40] for >99% ee $[\alpha]_D^{20}$ −95.9 (*c* 1.1, $CHCl_3$)} indicating that no racemisation occurs during the cleavage process (Scheme 20).



Scheme 20. Reagents and conditions: (i) HCl (10% aq), THF, rt, 12 h; (ii) HCl (10% aq), THF, reflux, 12 h; (iii) $NaIO_4$, $RuCl_3$, CCl_4/MeCN/H_2O (2:2:3); (iv) MeMgBr, MeOH.

3. Conclusion

In conclusion, the oxidation of SuperQuat enamides via epoxidation with DMDO and subsequent S_N1-type regio- and stereoselective epoxide opening with *m*-chlorobenzoic acid generates the corresponding 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives in good to excellent de, which can be recrystallised to single diastereoisomers (>98% de). Enamide oxidation with *m*CPBA generates the 1′-*m*-chlorobenzoyl-2′-hydroxy derivatives in one pot. Subsequent reductive cleavage enables access to 1,2-diols with high enantiomeric purity. The SuperQuat enamides are available with either (*E*)- or (*Z*)-geometry of the double bond, and therefore this protocol represents a stereodivergent strategy to either enantiomer of the corresponding 1,2-diol from a single enantiomer of the SuperQuat auxiliary. Alternatively, addition of a *C*(1′)-lithiated SuperQuat enamide to an aromatic aldehyde proceeds with high levels of diastereoselectivity. Sequential O-benzylation, enamide oxidation with $NaIO_4$/$RuCl_3$ and methanolysis give a homochiral *O*-benzyl protected α-hydroxy methyl ester in high ee.

4. Experimental

4.1. General experimental

All reactions involving organometallic or other moisture-sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs et al.[41] Water was purified by an Elix® UV-10 system. All other solvents were used as supplied (analytical or HPLC grade) without prior purification. *m*CPBA was used as a 70–77% suspension in water (Aldrich). Solutions of DMDO in acetone were prepared[15a] and titrated[15b] according to the procedures of Adam et al. Organic layers were dried over $MgSO_4$. Thin layer chromatography was performed on aluminium plates coated with 60 F_{254} silica. Plates were visualised using UV light (254 nm), iodine, 1% aq $KMnO_4$ or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed on Kieselgel 60 silica.

Elemental analyses were recorded by the microanalysis service of the Inorganic Chemistry Laboratory, University of Oxford, UK. Melting points were recorded on a Gallenkamp Hot Stage apparatus and are uncorrected. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter with a water-jacketed 10 cm cell. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g/100 mL. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer as either a thin film on NaCl plates (film) or a KBr disc (KBr), as stated. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded on Bruker Avance spectrometers in the deuterated solvent stated. The field was locked by external referencing to the relevant deuteron resonance. Low-resolution mass spectra were recorded on either a VG MassLab 20–250 or a Micromass Platform 1 spectrometer. The ion $[M+59]^+$ refers to $[M+MeCN+NH_4]^+$. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyalanine or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m×0.25 mm) using amyl acetate as a lock mass. Chiral gas chromatography was performed on a CE instruments Trace GC (Thermoquest) machine with an SGE Cydex-β stationary phase (25 m×0.22 mm) with helium as the carrier gas, using an FID detector.

4.2. General procedure 1 for the preparation of SuperQuat (*E*)-enamides

TsOH (ca. 25 mol %) and the requisite aldehyde (1.2 equiv) were added sequentially to a stirred solution of SuperQuat **13** (1.0 equiv) in PhMe. The reaction mixture was heated at 120 °C under Dean–Stark conditions for 12 h and then concentrated in vacuo. The residue was purified via flash column chromatography.

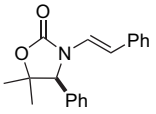
4.3. General procedure 2 for oxidation of SuperQuat enamides with *m*CPBA

*m*CPBA (1.5 equiv) was added to a stirred solution of the requisite SuperQuat enamide (1.0 equiv) in $CHCl_3$ at 0 °C and the resultant suspension stirred for 30 min before warming to rt over a further 2 h. After this time, satd aq Na_2SO_3 was added until starch–iodide paper indicated that no *m*CPBA remained. The mixture was then partitioned between DCM and satd aq NH_4Cl, and the organic layer was separated. The aqueous layer was then extracted twice with DCM and the combined organic extracts were washed twice with brine, dried and concentrated in vacuo. The residue was purified via recrystallisation from DCM/heptane (1:1).

4.4. General procedure 3 for addition of lithiated SuperQuat enamides to an aldehyde

^{t}BuLi (1.7 M in pentane, 2.0 equiv) was added dropwise via syringe to a solution of SuperQuat enamide **14** (1.0 equiv) in anhydrous THF at −78 °C and stirred for 45 min. The requisite aldehyde (2.2 equiv) was added and the reaction mixture was stirred for a further 1 h at −78 °C before the addition of BnBr (2.0 equiv), after which it was allowed to warm to rt over 12 h. The reaction mixture was quenched with satd aq NH_4Cl, diluted with H_2O and extracted three times with EtOAc. The combined organic extracts were dried and concentrated in vacuo. The residue was purified via flash column chromatography.

4.4.1. (S,E)-N(3)-(2′-Phenylethenyl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***14***

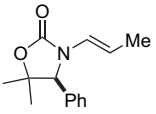


Following *General Procedure 1*, TsOH (ca. 500 mg), phenylacetaldehyde (1.47 mL, 12.6 mmol) and **13** (2.0 g, 10.5 mmol) in PhMe (150 mL) gave the crude reaction mixture. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 19:1) gave **14** as a white solid (2.43 g, 79%). Found C, 78.0; H, 6.5; N, 4.65%. $C_{19}H_{19}NO_2$ requires C, 77.8; H, 6.5; N, 4.8%. Mp 144 °C; $[\alpha]_D^{23}$ +7.8 (*c* 1.0, DCM); ν_{max} (DCM) 1752 (C=O); δ_H (200 MHz, $CDCl_3$) 1.00 (3H, s, C(5)*Me*$_A$), 1.66 (3H, s, C(5)*Me*$_B$), 4.81 (1H, s, C(4)*H*), 5.51 (1H, d, *J* 14.9, C(2′)*H*), 7.12–7.50 (11H, m, C(1′)*H*, *Ph*); δ_C (50 MHz, $CDCl_3$) 24.1, 29.2, 68.1, 82.6, 113.0, 123.4, 125.6, 126.8, 128.8, 129.1, 129.3, 135.0, 136.2, 155.2; *m*/*z* (APCI$^+$) 294 ($[M+H]^+$).

4.4.1.1. X-ray crystal structure determination for ***14****.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

X-ray crystal structure data for **14** [$C_{19}H_{19}NO_2$]: M=293.37, monoclinic, space group $P12_11$, a=6.1034(2) Å, b=7.9182(3) Å, c=17.0391(7) Å, β=92.994(2)°, V=822.34(5) Å^3, Z=2, μ=0.077 mm^{-1}, colourless plate, crystal dimensions=0.1×0.1×0.2 mm^3. A total of 1970 unique reflections were measured for $5<\theta<27$ and 1629 reflections were used in the refinement. The final parameters were wR_2=0.056 and R_1=0.047 [$I>1.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653128. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.4.2. (S,E)-N(3)-(Prop-1′-en-1′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***15***



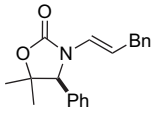
trans-1-Bromoprop-1-ene (0.81 mL, 9.40 mmol) was added to a suspension of **13** (360 mg, 1.88 mmol), CuI (30 mg, 0.156 mmol), K_2CO_3 (434 mg, 3.14 mmol) and *N*,*N*′-dimethylethylenediamine (17 μL, 0.156 mmol) in PhMe (3 mL). The suspension was stirred at

110 °C for 5 days then allowed to cool to rt, filtered through Celite (eluent EtOAc) and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 19:1) gave **15** as a white solid (432 mg, quant). Found C, 72.5; H, 7.3; N, 5.8%. $C_{14}H_{17}NO_2$ requires C, 72.7; H, 7.4; N, 6.1%. Mp 78–79 °C; $[\alpha]_D^{23}$ +93.3 (*c* 0.2, $CHCl_3$); ν_{max} (KBr) 1734 (C=O); δ_H (400 MHz, $CDCl_3$) 0.93 (3H, s, C(5)*Me*$_A$), 1.54 (3H, app ddd, *J* 6.8, 1.0, 0.8, C(3′)*H*$_3$), 1.59 (3H, s, C(5)*Me*$_B$), 4.46–4.56 (1H, m, C(2′)*H*), 4.58 (1H, s, C(4)*H*), 6.61–6.68 (1H, m, C(1′)*H*), 7.11–7.16 (2H, m, *Ph*), 7.32–7.42 (3H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 15.2, 24.1, 29.3, 68.3, 82.0, 107.8, 123.7, 128.6, 128.9, 135.2; *m*/*z* (ESI^+) 290 ($[M+59]^+$, 100%); HRMS (ESI^+) found 254.1157, $C_{14}H_{17}NNaO_2^+$ ($[M+Na]^+$) requires 254.1151.

4.4.2.1. X-ray crystal structure determination for ***15****.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

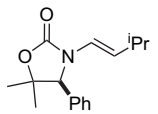
X-ray crystal structure data for **15** [$C_{14}H_{17}NO_2$]: *M*=231.29, orthorhombic, space group $P2_12_12_1$, *a*=7.7201(2) Å, *b*=9.8983(3) Å, *c*=17.1370(5) Å, *V*=1309.54(6) Å^3, *Z*=4, μ=0.078 mm^{-1}, colourless plate, crystal dimensions=0.05×0.1×0.1 mm^3. A total of 1703 unique reflections were measured for 5<θ<27 and 1316 reflections were used in the refinement. The final parameters were wR_2=0.051 and R_1=0.043 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653129. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.4.3. (S,E)-N(3)-(3′-Phenyl-prop-1′-enyl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***16****.*



Following *General Procedure 1*, TsOH (ca. 125 mg), 3-phenylpropionaldehyde (1.47 mL, 12.6 mmol) and **13** (500 mg, 2.62 mmol) in PhMe (35 mL) gave the crude reaction mixture. Purification via flash column chromatography (eluent 40–60 °C petrol/EtOAc, 15:1) gave **16** as a white solid (570 mg, 71%); $[\alpha]_D^{25}$ +38.4 (*c* 1.5, $CHCl_3$); ν_{max} (KBr) 1751 (C=O), 1670 (C=C); δ_H (400 MHz, $CDCl_3$) 0.95 (3H, s, C(5)*Me*$_A$), 1.61 (3H, s, C(5)*Me*$_B$), 3.18–3.31 (2H, m, C(3)*H*$_2$), 4.60–4.71 (2H, m, C(4)*H*, C(2′)*H*), 6.77 (1H, d, *J* 14.4, C(1′)*H*), 6.92–7.41 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.2, 29.3, 35.6, 68.2, 82.0, 111.8, 124.1 (2C), 125.8, 126.0, 126.1, 128.1, 128.2, 128.4, 128.5, 128.6, 128.7, 128.9, 129.2, 134.9, 140.4, 154.8; *m*/*z* ($APCI^+$) 308 ($[M+H]^+$, 20%), 264 (100), 192 (100); HRMS (ESI^+) found 308.1651, $C_{20}H_{22}NO_2^+$ ($[M+H]^+$) requires 308.1645.

4.4.4. (S,E)-N(3)-(3′-Methyl-but-1′-enyl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***17****.*

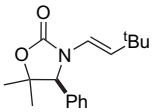


Following *General Procedure 1*, TsOH (ca. 100 mg), 3-methylbutyraldehyde (0.40 mL, 3.77 mmol) and **13** (300 mg, 1.57 mmol) in PhMe (25 mL) gave the crude reaction mixture. Purification via flash column chromatography (eluent 40–60 °C petrol/EtOAc/Et_3N, 75:25:1) gave **17** as a white solid (290 mg, 71%). Found C, 74.6; H, 8.45; N, 5.15%. $C_{16}H_{21}NO_2$ requires C, 74.7; H, 8.5; N, 5.1%. Mp 96–97 °C; $[\alpha]_D^{21}$ +91.7 (*c* 0.9, $CHCl_3$); ν_{max} (KBr) 1735 (C=O), 1669 (C=C); δ_H (400 MHz, $CDCl_3$) 0.80 (3H, d, *J* 6.7, C*H*$_3$CHCH$_3$), 0.85 (3H, d, *J* 6.7, CH$_3$CHC*H*$_3$), 0.94 (3H, s, C(5)*Me*$_A$), 1.60 (3H, s, C(5)*Me*$_B$), 2.17 (1H, *J* 6.9, 6.7, 1.2, CH$_3$C*H*CH$_3$), 4.46 (1H, dd, *J* 14.6, 6.9, C(2′)*H*), 4.60 (1H, s, C(4)*H*), 6.60 (1H, dd, *J* 14.6, 1.2, C(1′)*H*), 7.40–7.11 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 22.6, 22.8, 24.2, 29.0, 29.3, 68.2, 81.9, 120.8, 128.5, 128.7, 135.1, 155.0; *m*/*z* (CI^+) 260 ($[M+H]^+$, 6%), 216 (100).

4.4.4.1. X-ray crystal structure determination for ***17****.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

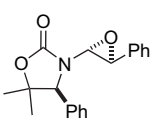
X-ray crystal structure data for **17** [$C_{16}H_{21}NO_2$]: *M*=259.35, orthorhombic, space group $P2_12_12_1$, *a*=9.8502(2) Å, *b*=10.3090(2) Å, *c*=14.3867(3) Å, *V*=1460.91(5) Å^3, *Z*=4, μ=0.077 mm^{-1}, colourless plate, crystal dimensions=0.3×0.4×0.5 mm^3. A total of 1895 unique reflections were measured for 5<θ<27 and 1660 reflections were used in the refinement. The final parameters were wR_2=0.039 and R_1=0.033 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653136. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.4.5. (S,E)-N(3)-(3′,3′-Dimethyl-but-1′-enyl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***18****.*



Following *General Procedure 1*, TsOH (ca. 100 mg), 3,3-dimethylbutyraldehyde (0.31 mL, 2.51 mmol) and **13** (400 mg, 2.09 mmol) in PhMe (40 mL) gave the crude reaction mixture. Purification via flash column chromatography (eluent 40–60 °C petrol/EtOAc/Et_3N, 100:10:1) gave **18** as a white solid (382 mg, 67%). Found C, 74.0; H, 8.1; N, 5.45%. $C_{17}H_{23}NO_2$ requires C, 74.1; H, 8.2; N, 5.4%. Mp 105–107 °C; $[\alpha]_D^{22}$ +83.5 (*c* 1.05, $CHCl_3$); ν_{max} (KBr) 1733 (C=O), 1669 (C=C); δ_H (400 MHz, $CDCl_3$) 0.85 (3H, s, C(5)*Me*$_A$), 0.94 (9H, s, C*Me*$_3$), 1.60 (3H, s, C(5)*Me*$_B$), 4.49 (1H, d, *J* 14.8, C(2′)*H*), 4.61 (1H, s, C(4)*H*), 6.56 (1H, d, *J* 14.8, C(1′)*H*), 7.38–7.10 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.2, 29.3, 29.8, 31.9, 68.2, 81.9, 119.4, 125.3, 128.4, 128.6, 135.0, 155.1; *m*/*z* (CI^+) 274 ($[M+H]^+$, 42%), 230 (100).

4.4.6. (4S,2′R,3′S)-N(3)-(3′-Phenyloxiran-2′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***19****.*



A solution of DMDO (0.116 M in acetone, 6.1 mL, 0.71 mmol) at 0 °C was added to **14** (100 mg, 0.34 mmol) and the reaction mixture allowed to warm to rt over 1 h (with stirring) before being concentrated in vacuo to give a mixture of products (105 mg) of which **19** was the major component. Recrystallisation from DCM/heptane

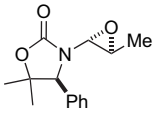
(1:1) gave **19** as a white solid (88 mg, 84%, >98% de). Found C, 74.0; H, 5.8; N, 4.3%. $C_{19}H_{19}NO_3$ requires C, 73.8; H, 6.2; N, 4.5%. Mp 92 °C; $[\alpha]_D^{21}$ −7.2 (*c* 0.5, $CHCl_3$); ν_{max} (KBr) 1773 (C=O); δ_H (400 MHz, $CDCl_3$) 0.81 (3H, s, C(5)*Me*$_A$), 1.56 (3H, s, C(5)*Me*$_B$), 3.55 (1H, s, C(3′)*H*), 4.49 (1H, s, C(4)*H*), 4.65 (1H, s, C(2′)*H*), 6.75–7.49 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.1, 28.8, 57.2, 65.6, 66.0, 82.5, 125.2, 126.8, 128.4, 128.6, 129.0, 129.2, 134.7, 136.4, 137.5; *m*/*z* (CI^+) 310 ($[M+H]^+$, 100%).

Epoxide opening. *m*CBA (80 mg, 0.51 mmol) was added to a solution of **19** (105 mg, ca. 0.34 mmol) in acetone (2 mL) at 0 °C, the resultant solution stirred for 30 min and then allowed to warm to rt over a further 2.5 h. The reaction mixture was concentrated in vacuo and the residue was partitioned between satd aq NH_4Cl (10 mL) and $CHCl_3$ (10 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (2×10 mL). The combined organic extracts were washed with brine (20 mL), dried and concentrated in vacuo to give a 96:4 mixture of **21**/**22** (159 mg, quant).

*4.4.6.1. X-ray crystal structure determination for **19**.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

X-ray crystal structure data for **19** [$C_{19}H_{19}NO_3$]: *M*=309.36, monoclinic, space group $P12_11$, *a*=8.241(1) Å, *b*=6.1420(7) Å, *c*=17.030(2) Å, *V*=860.8(2) Å^3, *Z*=2, μ=0.67 mm^{-1}, colourless plate, crystal dimensions=0.1×0.5×0.5 mm^3. A total of 2781 unique reflections were measured for 5<θ<27 and 1590 reflections were used in the refinement. The final parameters were wR_2=0.057 and R_1=0.045 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653144. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

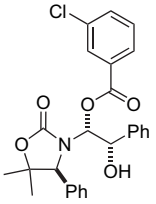
*4.4.7. (4S,2′R,3′S)-N(3)-(3′-Methyloxiran-2′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one **20***



A solution of DMDO (0.046 M in acetone, 19 mL, 0.87 mmol) at 0 °C was added to **15** (100 mg, 0.433 mmol) and the reaction mixture allowed to warm to rt over 1 h (with stirring) before being concentrated in vacuo to give **20** as a white solid (107 mg, quant, >98 % de) that was used without purification; δ_H (400 MHz, $CDCl_3$) 0.92 (3H, s, C(5)*Me*$_A$), 0.95 (3H, *J* 5.2, C(3′)*Me*), 1.56 (3H, s, C(5)*Me*$_B$), 2.77–2.78 (1H, m, C(3′)*H*), 4.40 (1H, s, C(4)*H*), 4.74 (1H, d, *J* 1.4, C(2′)*H*), 7.16–7.17 (2H, m, *Ph*), 7.35–7.43 (3H, m, *Ph*).

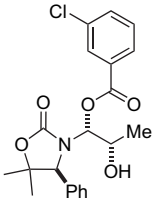
Epoxide opening. *m*CBA (102 mg, 0.65 mmol) was added to a solution of **20** (107 mg, 0.43 mmol, >98% de) in acetone (2.0 mL) at 0 °C, the resultant solution stirred for 30 min and then allowed to warm to rt over a further 2.5 h. The reaction mixture was concentrated in vacuo and the residue was partitioned between satd aq NH_4Cl (10 mL) and $CHCl_3$ (10 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (2×10 mL). The combined organic extracts were washed with brine (20 mL), dried and concentrated in vacuo to give **23** as a white solid (175 mg, quant, >98% de).

*4.4.8. (4S,1′R,2′S)-N(3)-[1′-(m-Chlorobenzoyl)-2′-hydroxy-2′-phenyl-ethan-1′-yl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one **21***



Following *General Procedure 2*, *m*CPBA (221 mg, 1.28 mmol) and **14** (150 mg, 0.51 mmol) in $CHCl_3$ (10 mL) gave a 96:4 mixture of **21**/**22**. Purification via recrystallisation from DCM/heptane (1:1) gave **21** as a white crystalline solid (200 mg, 84%, >98% de); mp 104–105 °C; $[\alpha]_D^{21}$ +94.0 (*c* 1.0, $CHCl_3$); ν_{max} (KBr) 1757 (C=O), 1736 (C=O); δ_H (400 MHz, $CDCl_3$) 0.82 (3H, s, C(5)*Me*$_A$), 0.98 (3H, s, C(5)*Me*$_B$), 2.64 (1H, br s, O*H*), 3.94 (1H, s, C(4)*H*), 5.66 (1H, d, *J* 7.7, C(2′)*H*), 6.24 (1H, d, *J* 7.7, C(1′)*H*), 6.84–8.03 (14H, m, *Ar*, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.4, 27.9, 71.4, 72.7, 82.3, 82.7, 127.3, 128.3, 128.4, 128.7, 129.0, 129.2, 129.5, 130.0, 130.4, 131.2, 133.7, 134.7, 135.5, 139.4, 156.7, 164.0; *m*/*z* (ESI^+) 488 ($[M+Na]^+$, 100%); HRMS (ESI^+) found 488.1232, $C_{26}H_{24}ClNNaO_5^+$ ($[M+Na]^+$) requires 488.1235.

*4.4.9. (4S,1′R,2′S)-N(3)-[1′-(m-Chlorobenzoyl)-2′-hydroxy-propan-1′-yl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one **23***



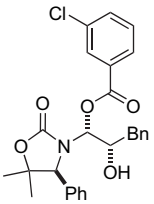
Following *General Procedure 2*, *m*CPBA (204 mg, 1.19 mmol) and **15** (153 mg, 0.66 mmol) in $CHCl_3$ (10 mL) gave a >99:<1 mixture of **23**/**24**. Purification via recrystallisation from DCM/heptane (1:1) gave **23** as a white crystalline solid (254 mg, 95%, >98% de); mp 72–73 °C; $[\alpha]_D^{17}$ +76.9 (*c* 0.7, $CHCl_3$); ν_{max} (KBr) 3441 (O–H), 1748 (C=O); δ_H (400 MHz, $CDCl_3$) 0.97 (3H, s, C(5)*Me*$_A$), 1.23 (3H, d, *J* 6.6, C(3′)*H*$_3$), 1.53 (3H, s, C(5)*Me*$_B$), 2.65 (1H, br s, O*H*), 4.16–4.22 (1H, m, C(2′)*H*), 4.52 (1H, s, C(4)*H*), 6.27 (1H, d, *J* 5.1, C(1′)*H*), 7.15–7.90 (9H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 19.3, 23.5, 28.7, 67.1, 69.3, 82.4, 83.1, 128.0, 128.8, 128.9, 129.7, 129.8, 130.7, 133.5, 134.5, 136.3, 157.0, 163.8; *m*/*z* (ESI^+) 462 ($[M+59]^+$, 100%); HRMS (ESI^+) found 426.1077, $C_{21}H_{22}ClNNaO_5^+$ ($[M+Na]^+$) requires 426.1079.

*4.4.9.1. X-ray crystal structure determination for **23**.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

X-ray crystal structure data for **23** [$C_{21}H_{21}ClNO_5$]: *M*=402.85, orthorhombic, space group $P2_12_12_1$, *a*=7.22210(10) Å, *b*=11.8317(2) Å, *c*=24.1532(4) Å, *V*=2063.88(6) Å^3, *Z*=4, μ=0.22 mm^{-1}, colourless block, crystal dimensions=0.3×0.3×0.3 mm^3. A total of 4442 unique reflections were measured for 5<θ<27 and 3864 reflections were used in the refinement. The final parameters were wR_2=0.077 and R_1=0.064 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number

CCDC 653133. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.4.10. (4S,1′R,2′S)-N(3)-(1′-m-Chlorobenzoyl-2′-hydroxy-3′-phenyl-prop-1′-yl-)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***25***

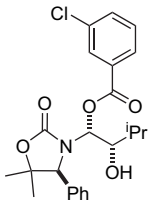


Following *General Procedure 2*, *m*CPBA (471 mg, 2.83 mmol) and **16** (300 mg, 0.98 mmol) in $CHCl_3$ (40 mL) gave a 96:4 mixture of **25**/**26**. Recrystallisation from DCM/heptane (1:1) gave **25** as a white crystalline solid (280 mg, 60%, >98% de). Found C, 67.8; H, 5.4; N, 2.7%. $C_{27}H_{26}ClNO_5$ requires C, 67.6; H, 5.4; N, 2.9%. Mp 109–110 °C; $[\alpha]_D^{25}$ +68.6 (*c* 1.0, $CHCl_3$); ν_{max} (KBr) 3455 (O–H), 1736 (C=O); δ_H (400 MHz, $CDCl_3$) 0.97 (3H, s, C(5)*Me*$_A$), 1.53 (3H, s, C(5)*Me*$_B$), 2.72 (1H, dd, *J* 13.9, 8.9, C(3′)*H*$_A$), 2.89 (1H, dd, *J* 13.9, 4.1, C(3′)*H*$_B$), 4.20 (1H, br m, C(2′)*H*), 4.50 (1H, s, C(4)*H*), 6.44 (1H, d, *J* 5.3, C(1′)*H*), 7.92–7.01 (14H, m, *Ar*, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.4, 28.8, 39.3, 68.7, 71.9, 81.1, 83.2, 126.7, 128.0, 128.5, 128.9, 129.3, 129.7, 129.8, 130.7, 133.5, 134.5, 136.5, 136.8, 157.1, 163.7; *m*/*z* (ESI$^+$) 502 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) found 502.1389, $C_{27}H_{26}ClNNaO_5^+$ ([M+Na]$^+$) requires 502.1392.

4.4.10.1. X-ray crystal structure determination for ***25****.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

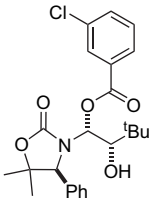
X-ray crystal structure data for **25** [$C_{27}H_{26}ClNO_5$]: *M*=479.96, triclinic, space group *P*1, *a*=6.1400(2) Å, *b*=8.1370(2) Å, *c*=12.9972(5) Å, α=104.1148(11)°, β=102.6525(11)°, γ=94.8880(15)°, *V*=607.83(3) Å^3, *Z*=1, μ=0.20 mm^{-1}, colourless block, crystal dimensions=0.2×0.2×0.2 mm^3. A total of 5047 unique reflections were measured for $1<\theta<27$ and 3965 reflections were used in the refinement. The final parameters were wR_2=0.019 and R_1=0.034 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653137. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.4.11. (4S,1′R,2′S)-N(3)-(1′-m-Chlorobenzoyl-2′-hydroxy-3′-methyl-but-1′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***27****.*



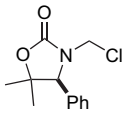
Following *General Procedure 2*, *m*CPBA (62 mg, 0.36 mmol) and **17** (37 mg, 0.14 mmol) in $CHCl_3$ (7 mL) gave a 96:4 mixture of **27**/**28**. Recrystallisation from DCM/heptane (1:1) gave **27** as a white crystalline solid (200 mg, 61%, >98% de); ν_{max} (KBr) 3447 (O–H), 1750 (C=O); δ_H (400 MHz, $CDCl_3$) 0.81 (3H, d, *J* 6.8, C*H*$_3$CHCH$_3$); 0.96 (3H, d, *J* 6.8, CH$_3$CHC*H*$_3$), 0.97 (3H, s, C(5)*Me*$_A$), 1.51 (3H, s, C(5)*Me*$_B$), 1.78 (1H, m, CH$_3$C*H*CH$_3$), 2.58 (1H, br s, O*H*), 3.81 (1H, dd, *J* 6.8, 5.8, C(2′)*H*), 4.53 (1H, s, C(4)*H*), 6.49 (1H, d, *J* 5.8, C(1′)*H*), 8.13–7.16 (9H, m, *Ar*, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.1, 19.4, 23.4, 28.8, 29.5, 68.8, 74.9, 80.2, 83.0, 127.3, 128.1, 128.9, 129.7, 130.2, 130.9, 133.5, 134.4, 134.6, 136.5, 157.0, 163.8; *m*/*z* (ESI$^+$) 454 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) found 454.1396, $C_{23}H_{26}ClNNaO_5^+$ ([M+Na]$^+$) requires 454.1392.

4.4.12. (4S,1′R,2′S)-N(3)-(1′-m-Chlorobenzoyl-2′-hydroxy-3′,3′-dimethyl-but-1′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***29****.*



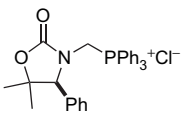
Following *General Procedure 2*, *m*CPBA (317 mg, 1.84 mmol) and **18** (200 mg, 0.73 mmol) in $CHCl_3$ (10 mL) gave a 98:2 mixture of **29**/**30** as a yellow oil (359 mg, quant, 96% de) that was used without purification; ν_{max} (film) 3433 (O–H), 1730 (C=O); δ_H (400 MHz, $CDCl_3$) 0.92 (9H, s, C*Me*$_3$), 0.93 (3H, s, C(5)*Me*$_A$), 1.51 (3H, s, C(5)*Me*$_B$), 3.63 (1H, d, *J* 1.1, C(2′)*H*), 4.53 (1H, s, C(4)*H*), 6.57 (1H, d, *J* 1.1, C(1′)*H*), 7.15–8.09 (9H, m, *Ar*, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.3, 26.0, 28.6, 34.6, 69.5, 77.3, 78.7, 83.2, 128.0, 128.7, 129.0, 129.7, 129.8, 130.1, 133.4, 134.5, 136.4, 157.3, 163.3; *m*/*z* (ESI$^+$) 468 ([M+Na]$^+$, 100%).

4.4.13. (S)-N(3)-Chloromethyl-4-phenyl-5,5-dimethyl-oxazolidin-2-one.



A suspension of **13** (1.06 g, 5.55 mmol) and paraformaldehyde (1.16 g, 6.09 mmol) in TMSCl (8.9 mL) was refluxed at 60 °C for 2 h. The volatile materials were then removed in vacuo to give the title compound as a yellow solid (1.33 g, quant) that was used without purification; mp 161–162 °C; $[\alpha]_D^{22}$ +135.7 (*c* 0.9, $CHCl_3$); ν_{max} (film) 1766 (C=O); δ_H (400 MHz, $CDCl_3$) 1.00 (3H, s, C(5)*Me*$_A$), 1.60 (3H, s, C(5)*Me*$_B$), 4.67 (1H, d, *J* 10.3, C(1′)*H*$_A$), 4.75 (1H, s, C(4)*H*), 5.75 (1H, d, *J* 10.3, C(1′)*H*$_B$), 7.20–7.25 (2H, m, *Ph*), 7.40–7.49 (3H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.8, 27.9, 55.0, 67.0, 82.6, 127.0, 129.2, 129.3, 133.3, 156.5; *m*/*z* (ESI$^+$) 204 ([M−Cl]$^+$, 100%).

4.4.14. (S)-N(3)-[(Triphenylphosphonium)methyl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one chloride ***31****.*



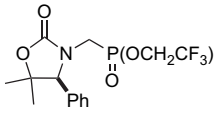
PPh_3 (26.9 g, 103 mmol) was added to a stirred suspension of freshly prepared (*S*)-*N*(3)-chloromethyl-4-phenyl-5,5-dimethyl-oxazolidin-2-one (12.5 g, 521 mmol) in MeCN (192 mL) and the suspension stirred at rt for 24 h. The reaction mixture was then concentrated in vacuo and the residue was purified via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 9:1) to give **31** as a white solid (19.4 g, 74%); mp 143–144 °C; $[\alpha]_D^{20}$ +30.4 (*c* 0.8, $CHCl_3$); ν_{max} (KBr) 1744 (C=O); δ_H (400 MHz, $CDCl_3$) 0.85 (3H, s, C(5)*Me*$_A$), 1.37 (3H, s, C(5)*Me*$_B$), 5.31 (1H, s, C(4)*H*), 5.59 (1H, dd, *J* 12.1, 6.1, C(1′)*H*$_A$), 5.68 (1H, dd, *J* 12.1, 3.5, C(1′)*H*$_B$), 7.14 (2H, s, *Ph*), 7.28–7.32 (3H, m, *Ph*), 7.64–7.90 (15H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 23.8, 28.3, 41.0 (d, *J* 60.1), 69.6, 84.3, 117.2, 117.9, 129.1, 129.1, 130.3,

130.4, 134.2, 134.3, 134.6, 135.1, 135.1, 158.5; *m/z* (ESI$^+$) 466 ([M−Cl]$^+$, 100%); HRMS (ESI$^+$) found 466.1931, $C_{30}H_{29}NO_2P^+$ ([M−Cl]$^+$) requires 466.1930.

4.4.14.1. X-ray crystal structure determination for ***31****.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

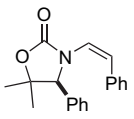
X-ray crystal structure data for **31** [$C_{61}H_{60}Cl_4N_2O_4P_2$]: M=1088.92, orthorhombic, space group $P2_12_12_1$, a=15.9103(2) Å, b=18.3528(3) Å, c=18.9501(2) Å, V=5533.40(13) Å^3, Z=8, μ=0.32 mm^{-1}, colourless block, crystal dimensions=0.2×0.2×0.2 mm^3. A total of 12,429 unique reflections were measured for $5<\theta<27$ and 8956 reflections were used in the refinement. The final parameters were wR_2=0.041 and R_1=0.042 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653130. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.4.15. (S)-N(3)-[(Bis-2″,2″,2″-trifluoroethoxyphosphoryl)methyl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***32***



A mixture of tris-(2,2,2-trifluoroethyl)phosphite (627 μL, 2.40 mmol) and freshly prepared (*S*)-*N*(3)-chloromethyl-4-phenyl-5,5-dimethyl-oxazolidin-2-one (480 mg, 2.00 mmol) was heated at 140 °C for 72 h. The reaction mixture was then allowed to cool to rt and concentrated in vacuo. The residue was purified via flash column chromatography (eluent 30–40 °C petrol and then 30–40 °C petrol/Et_2O, 5:1) to give **32** as a colourless oil (533 mg, 64%). Found C, 42.7; H, 4.3; N, 3.1%. $C_{16}H_{18}F_6NO_5P$ requires C, 42.8; H, 4.0; N, 3.1%. $[\alpha]_D^{24}$ +49.9 (*c* 1.0, $CHCl_3$); ν_{max} (film) 1749 (C=O); δ_H (400 MHz, $CDCl_3$) 0.97 (3H, s, C(5)Me_A), 1.59 (3H, s, C(5)Me_B), 3.19 (1H, dd, *J* 16.4, 6.3, C(1′)H_A), 4.22 (1H, dd, *J* 16.4, 12.1, C(1′)H_B), 4.35–4.50 (4H, m, 2×OCH_2), 4.64 (1H, app d, *J* 2.0, C(4)*H*), 7.10–7.14 (2H, m, *Ph*), 7.37–7.45 (3H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.8, 28.5, 39.0, 62.3 (quintet, P(OCH_2CF_3)$_2$), 69.6, 82.6, 121.0–121.1 (m, (CF_3)$_A$), 123.7–123.8 (m, (CF_3)$_B$), 129.2, 129.4, 133.8, 157.3; *m/z* (ESI$^+$) 472 ([M+Na]$^+$, 24%); HRMS (FI$^+$) found 449.0827, $C_{16}H_{18}F_6NO_5P^+$ ([M]$^+$) requires 449.0821.

4.4.16. (S,Z)-N(3)-(2′-Phenyl-ethenyl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***33***



Wittig olefination. A suspension of KO^{t}Bu (14 mg, 0.13 mmol) in THF (1 mL) was added to a stirred suspension of **31** (50 mg, 0.1 mmol) in THF (1 mL) at −78 °C. After 30 min, PhCHO (50 μL, 0.5 mmol) was added and stirring continued for a further 24 h at −78 °C. The reaction mixture was quenched with satd aq NH_4Cl (1 mL) and allowed to warm to rt. The organic layer was separated and the aqueous layer extracted with DCM (2×5 mL). The combined organic extracts were washed with brine (5 mL), dried and concentrated in vacuo to give a 9:91 mixture of **14**/**33**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 19:1) gave **33** as a white solid (22 mg, 76%, >98% de). Found C, 77.7; H, 6.6; N, 4.7%. $C_{19}H_{19}NO_2$ requires C, 77.8; H, 6.5; N, 4.8%. Mp 105–106 °C; $[\alpha]_D^{24}$ +40.0 (*c* 0.8, $CHCl_3$); ν_{max} (KBr) 1745 (C=O); δ_H (400 MHz, $CDCl_3$) 0.86 (3H, s, C(5)Me_A), 1.55 (3H, s, C(5)Me_B), 4.43 (1H, s, C(4)*H*), 5.85 (1H, d, *J* 9.6, C(2′)*H*), 6.55 (2H, m, *Ph*), 6.62 (1H, d, *J* 9.6, C(1′)*H*), 6.95–6.99 (2H, m, *Ph*), 7.11–7.30 (6H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.8, 28.8, 68.8, 82.4, 115.5, 123.1, 125.4, 127.1, 127.8, 128.3, 128.6, 129.2, 135.3, 135.7, 156.6; *m/z* (ESI$^+$) 294 ([M+H]$^+$, 38%); HRMS (ESI$^+$) found 294.1500; $C_{19}H_{20}NO_2^+$ ([M+H]$^+$) requires 294.1489.

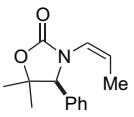
Wittig olefinations employing **31** were found to be highly sensitive to the presence of adventitious water, with (*S*)-*N*(3)-methyl-4-phenyl-5,5-dimethyl-oxazolidin-2-one (*N*-methyl SuperQuat) being isolated as a side product on several occasions; mp 90–91 °C; $[\alpha]_D^{24}$ +78.2 (*c* 0.3, $CHCl_3$); ν_{max} (KBr) 1735 (C=O); δ_H (400 MHz, $CDCl_3$) 0.92 (3H, s, C(5)Me_A), 1.57 (3H, s, C(5)Me_B), 2.79 (3H, s, N*Me*), 4.37 (1H, s, C(4)*H*), 7.15–7.19 (2H, m, *Ph*), 7.35–7.44 (3H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.8, 29.3, 31.3, 72.2, 83.6, 130.1, 130.2, 131.4, 157.8; *m/z* (ESI$^+$) 264 ([M+59]$^+$, 100%); HRMS (ESI$^+$) found 206.1186, $C_{12}H_{16}NO_2^+$ ([M+H]$^+$) requires 206.1176.

Still–Gennari olefination. BuLi (2.5 M in hexanes, 0.19 mL, 0.48 mmol) was added to a stirred suspension of **32** (100 mg, 0.24 mmol) in THF (2 mL) at −78 °C. After stirring for 30 min, PhCHO (24 μL, 0.24 mmol) was added and stirring continued at −78 °C for 24 h. The reaction mixture was then allowed to warm to rt, quenched with H_2O (1 mL) and extracted with DCM (3×10 mL). The combined organic extracts were then washed with brine (2×20 mL), dried and concentrated in vacuo. Purification of the residue via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 19:1) gave **33** as a white solid (70 mg, quant).

4.4.16.1. X-ray crystal structure determination for ***33****.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

X-ray crystal structure data for **33** [$C_{19}H_{19}NO_2$]: M=293.37, orthorhombic, space group $P2_12_12_1$, a=6.9994(2) Å, b=9.6521(3) Å, c=23.7351(6) Å, V=1603.52(8) Å^3, Z=4, μ=0.079 mm^{-1}, colourless plate, crystal dimensions=0.05×0.1×0.2 mm^3. A total of 2046 unique reflections were measured for $5<\theta<27$ and 1666 reflections were used in the refinement. The final parameters were wR_2=0.045 and R_1=0.042 [$I>1.5\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653131. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.4.17. (S,Z)-N(3)-(Prop-1′-en-1′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one ***34***



Wittig olefination. A suspension of KO^{t}Bu (28 mg, 0.25 mmol) in THF (2 mL) was added to a stirred suspension of **31** (100 mg, 0.2 mmol) in THF (2 mL) at −78 °C. After 30 min, MeCHO (56 μL, 1.0 mmol) was added and stirring continued for a further 24 h at −78 °C. The reaction mixture was quenched with satd aq NH_4Cl

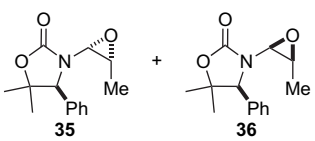
(1 mL) and allowed to warm to rt. The organic layer was separated and the aqueous layer extracted with DCM (2×10 mL). The combined organic extracts were washed with brine (10 mL), dried and concentrated in vacuo to give a 20:80 mixture of **15**/**34**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 19:1) gave **34** as a white solid (28 mg, 63%, >98% de); mp 82–83 °C; $[\alpha]_D^{24}$ +39.9 (*c* 0.9, $CHCl_3$); ν_{max} (KBr) 1753 (C=O); δ_H (400 MHz, $CDCl_3$) 0.96 (3H, s, C(5)Me_A), 1.61 (3H, dd, *J* 5.6, 1.8, C(3′)H_3), 1.64 (3H, s, C(5)Me_B), 4.73 (1H, s, C(4)*H*), 5.08 (1H, m, C(2′)*H*), 5.97 (1H, dq, *J* 7.1, 1.8, C(1′)*H*), 7.12–7.15 (2H, m, *Ph*), 7.34–7.41 (3H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.9, 23.9, 28.7, 70.7, 81.9, 116.2, 122.9, 128.7, 128.8, 135.8, 155.9; *m*/*z* (ESI$^+$) 232 ([M+H]$^+$, 65%); HRMS (ESI$^+$) found 232.1338, $C_{14}H_{18}NO_2$ ([M+H]$^+$) requires 232.1332.

Buchwald–Hartwig coupling. *cis*-1-Bromo-prop-1-ene (0.92 mL, 10.9 mmol) was added to a suspension of **13** (500 mg, 2.61 mmol), CuI (41 mg, 0.22 mmol), K_2CO_3 (600 mg, 4.35 mmol) and *N*,*N*′-dimethylethylenediamine (23 μL, 0.22 mmol) in PhMe (5 mL). The suspension was stirred at 110 °C for 5 days. The reaction mixture was then allowed to cool to rt and filtered through Celite (eluent EtOAc). The filtrate was concentrated in vacuo and the residue was purified via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 19:1) to give **34** as a white solid (603 mg, quant).

*4.4.17.1. X-ray crystal structure determination for **34***. Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

X-ray crystal structure data for **34** [$C_{14}H_{17}NO_2$]: *M*=231.29, monoclinic, space group $P12_11$, *a*=7.8226(2) Å, *b*=8.5396(2) Å, *c*=9.7413(4) Å, β=95.1000(10)°, *V*=648.16(3) Å^3, *Z*=2, μ=0.079 mm^{-1}, colourless plate, crystal dimensions=0.1×0.3×0.3 mm^3. A total of 1523 unique reflections were measured for 5<θ<27 and 1401 reflections were used in the refinement. The final parameters were wR_2=0.041 and R_1=0.041 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653132. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

*4.4.18. (4S,2′R,3′R)- and (4S,2′S,3′S)-N(3)-(3′-Methyloxiran-2′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one (4S,2′R,3′R)-**35** and (4S,2′S,3′S)-**36***



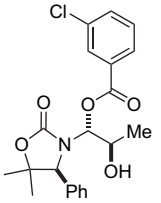
35 **36**

A solution of DMDO (0.046 M in acetone, 19 mL, 0.87 mmol) at 0 °C was added to **34** (42 mg, 0.18 mmol) and the reaction mixture allowed to warm to rt over 1 h (with stirring) before being concentrated in vacuo to give an 87:13 mixture of **35**/**36** (107 mg, quant) that was used without purification.

Data for **35**: δ_H (400 MHz, $CDCl_3$) 0.97 (3H, s, C(5)Me_A), 1.41 (3H, *J* 5.6, C(3′)H_3), 1.57 (3H, s, C(5)Me_B), 3.04–3.09 (1H, m, C(3′)*H*), 4.36 (1H, d, *J* 3.4, C(2′)*H*), 4.71 (1H, s, C(4)*H*), 7.16–7.24 (2H, m, *Ph*), 7.35–7.45 (3H, m, *Ph*).

Epoxide opening. *m*CBA (100 mg, 0.65 mmol) was added to a solution of the crude mixture of **35** and **36** (92 mg, 0.43 mmol, 87:13 dr) in acetone (2 mL) at 0 °C, and the resultant solution stirred for 30 min and then allowed to warm to rt over a further 2.5 h. The reaction mixture was concentrated in vacuo and the residue was partitioned between satd aq NH_4Cl (10 mL) and $CHCl_3$ (10 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (2×10 mL). The combined organic extracts were washed with brine (20 mL), dried and concentrated in vacuo to give to give a 5:8:84:3 mixture of **23**/**24**/**37**/**38** (175 mg, quant).

*4.4.19. (4S,1′R,2′R)-3-[1′-(m-Chlorobenzoyl)-2′-hydroxy-propan-1′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one **37***

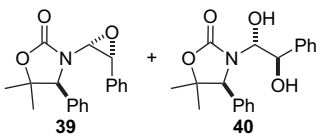


Following *General Procedure 2*, *m*CPBA (1.21 g, 5.41 mmol) and **34** (1.0 g, 4.33 mmol) in $CHCl_3$ (45 mL) gave a 7:10:81:2 mixture of **23**/**24**/**37**/**38**. Purification via recrystallisation from DCM/heptane (1:1) gave **37** as a white crystalline solid (718 mg, 41%, >98% de); mp 103–104 °C; $[\alpha]_D^{21}$ +64.6 (*c* 0.4 in $CHCl_3$); ν_{max} (KBr) 3406 (O–H), 1742 (C=O); δ_H (400 MHz, $CDCl_3$) 0.99 (3H, s, C(5)Me_A), 1.21 (3H, d, *J* 6.6, C(3′)H_3), 1.55 (3H, s, C(5)Me_B), 4.16–4.24 (1H, m, C(2′)*H*), 4.48 (1H, s, C(4)*H*), 6.11 (1H, d, *J* 7.6, C(1′)*H*), 7.11–8.09 (9H, m, *Ar*, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.3, 23.5, 29.0, 66.2, 69.6, 82.9, 83.2, 125.8, 128.0, 129.0, 129.1, 129.7, 129.8, 133.6, 134.6, 136.3, 145.7, 163.3; *m*/*z* (ESI$^+$) 462 ([M+59]$^+$, 100%); HRMS (ESI$^+$) found 426.1084, $C_{21}H_{22}ClNNaO_5^+$ ([M+Na]$^+$) requires 426.1079.

*4.4.19.1. X-ray crystal structure determination for **37***. Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

X-ray crystal structure data for **37** [$C_{21}H_{22}ClNO_5$]: *M*=403.86, orthorhombic, space group $P2_12_12_1$, *a*=5.5331(1) Å, *b*=10.7791(2) Å, *c*=33.3743(8) Å, *V*=1990.50(7) Å^3, *Z*=4, μ=0.22 mm^{-1}, colourless plate, crystal dimensions=0.05×0.1×0.2 mm^3. A total of 4293 unique reflections were measured for 5<θ<27 and 2707 reflections were used in the refinement. The final parameters were wR_2=0.041 and R_1=0.039 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653134. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

*4.4.20. (4S,2′R,3′R)-N(3)-(3′-Phenyloxiran-2′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one **39** and (4S,2′R,3′R)-N(3)-(1′,2′-dihydroxy-2′-phenylethyl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one **40***



39 **40**

A solution of DMDO (0.046 M in acetone, 15 mL, 0.69 mmol) at 0 °C was added to **33** (100 mg, 0.34 mmol) and the reaction mixture allowed to warm to rt over 1 h (with stirring) before being concentrated in vacuo to give a mixture of products (105 mg) of which

39 and **40** were the major components, in a 93:7 ratio. Recrystallisation of an aliquot from DCM/heptane (1:1) gave **40** as a white solid.

Data for **39**: δ_H (400 MHz, $CDCl_3$) 0.75 (3H, s, C(5)Me_A), 1.25 (3H, s, C(5)Me_B), 3.40 (1H, s, C(4)*H*), 3.97 (1H, d, *J* 3.4, C(3′)*H*), 4.76 (1H, d, *J* 5.5, C(2′)*H*), 7.21–7.49 (10H, m, *Ph*).

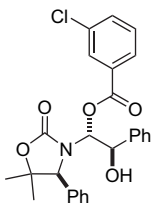
Data for **40**: mp 135–136 °C; $[\alpha]_D^{17}$ +58.0 (*c* 0.3, $CHCl_3$); ν_{max} (KBr) 3417 (O–H), 1723 (C=O); δ_H (400 MHz, $CDCl_3$) 0.83 (3H, s, C(5)Me_A), 1.15 (3H, s, C(5)Me_B), 3.94 (1H, s, C(4)*H*), 4.41 (1H, d, *J* 10.4, O*H*), 4.60–4.72 (2H, m, C(2′)*H*, O*H*), 5.02 (1H, dd, *J* 8.6, 5.8, C(1′)*H*), 6.85–7.63 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.9, 28.5, 70.0, 71.8, 82.0, 83.5, 126.1, 127.6, 128.2, 128.4, 129.1, 135.1, 139.9, 165.7; *m*/*z* (ESI^+) 328 ($[M+H]^+$, 62%); HRMS (ESI^+) found 328.1543, $C_{19}H_{22}NO_4^+$ ($[M+H]^+$) requires 328.1543.

Epoxide opening. *m*CBA (100 mg, 0.64 mmol) was added to a solution of the crude mixture of **39** and **40** (105 mg, ca. 0.34 mmol) in acetone (2 mL) at 0 °C, and the resultant solution stirred for 30 min and then allowed to warm to rt over a further 2.5 h. The reaction mixture was concentrated in vacuo and the residue was partitioned between satd aq NH_4Cl (10 mL) and $CHCl_3$ (10 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (2×10 mL). The combined organic extracts were washed with brine (20 mL), dried and concentrated in vacuo to give a 3:8:85:4 mixture of **21**/**22**/**41**/**42** (209 mg, quant).

*4.4.20.1. X-ray crystal structure determination for **40**.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92), all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

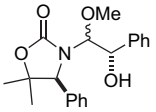
X-ray crystal structure data for **40** [$C_{19}H_{21}NO_4$]: M=327.38, monoclinic, space group $P12_11$, a=10.6588(4) Å, b=6.2394(3) Å, c=12.6433(5) Å, β=99.781(3)°, V=828.62(6) Å^3, Z=2, μ=0.092 mm^{-1}, colourless plate, crystal dimensions=0.1×0.1×0.2 mm^3. A total of 2017 unique reflections were measured for $5<\theta<27$ and 2017 reflections were used in the refinement. The final parameters were wR_2=0.073 and R_1=0.053 [$I>-3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 679091. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

*4.4.21. (4S,1′R,2′R)-N(3)-[1′-(m-Chlorobenzoyl)-2′-hydroxy-2′-phenylethan-1′-yl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one **41***



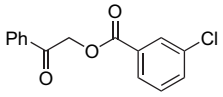
Following *General Procedure 2*, *m*CPBA (279 mg, 1.62 mmol) and **33** (230 mg, 1.37 mmol) in $CHCl_3$ (14 mL) gave a 5:14:77:4 mixture of **21**/**22**/**41**/**42**. Purification via recrystallisation from DCM/heptane (1:1) gave **41** as a white crystalline solid (207 mg, 57%, >98% de); mp 63–64 °C; $[\alpha]_D^{17}$ +44.7 (*c* 1.0, $CHCl_3$); ν_{max} (KBr) 1733 (C=O); δ_H (400 MHz, $CDCl_3$) 0.90 (3H, s, C(5)Me_A), 1.23 (3H, s, C(5)Me_B), 4.11 (1H, s, C(4)*H*), 4.54 (1H, d, *J* 7.9, O*H*), 5.24 (1H, m, C(2′)*H*), 6.16 (1H, d, *J* 6.6, C(1′)*H*), 7.06–7.81 (14H, m, *Ar*, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.5, 28.4, 65.8, 71.8, 82.1, 83.4, 126.0, 127.9, 128.2, 128.6, 128.8, 129.1, 129.7, 129.7, 130.6, 133.4, 134.5, 135.2, 139.4, 158.0, 163.0; *m*/*z* (ESI^+) 524 ($[M+59]^+$, 100%); HRMS (ESI^+) found 488.1236, $C_{26}H_{24}ClNNaO_5^+$ ($[M+Na]^+$) requires 488.1235.

*4.4.22. (4S,1′R,2′S)- and (4S,1′S,2′S)-N(3)-(1′-Methoxy-2′-hydroxy-2′-phenylethan-1′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one **43** and **44***



CSA (~5 mg) was added to a stirred solution of **21** (300 mg, 0.64 mmol) in MeOH (4 mL) and heated at reflux for 1 h. The reaction mixture was allowed to cool to rt and concentrated in vacuo. The residue was partitioned between DCM (5 mL) and H_2O (5 mL). The organic layer was separated and washed sequentially with satd aq $NaHCO_3$ (5 mL) and brine (5 mL), dried and concentrated in vacuo to give a 62:38 mixture of **43**/**44** (194 mg, 88%). Recrystallisation of an aliquot from EtOAc/pentane (1:1) gave the major diastereoisomer **43** of unknown configuration (>95% de) as a white solid. Found C, 70.4; H, 6.8; N, 4.1%. $C_{20}H_{23}NO_4$ requires C, 70.0; H, 6.7; N, 3.8%. Mp 92 °C; ν_{max} ($CHCl_3$) 1736 (C=O); δ_H (200 MHz, $CDCl_3$) 0.91 (3H, s, C(5)Me_A), 1.18 (3H, s, C(5)Me_B), 3.19 (3H, s, O*Me*), 3.32 (1H, br s, O*H*), 4.72 (1H, s, C(4)*H*), 4.92 (1H, d, *J* 6.4, C(2′)*H*), 5.15 (1H, d, *J* 6.4, C(1′)*H*), 7.19–7.45 (10H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 23.6, 28.1, 56.9, 67.1, 72.8, 82.4, 87.9, 126.4, 127.2, 127.8, 128.2, 128.4, 128.6, 137.2, 139.6, 158.8; *m*/*z* ($APCI^+$) 364 ($[M+Na]^+$, 100%).

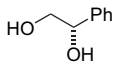
*4.4.23. 2-Oxo-2-phenylethyl m-chlorobenzoate **48***



Et_3N (cat) and DMAP (cat) were added sequentially to a stirred solution of **21** (41 mg, 0.09 mmol) in DCM (2 mL) at rt. After 12 h, the reaction mixture was concentrated in vacuo. Purification via flash column chromatography (eluent 40–60 °C petrol/EtOAc, 7:3) gave SuperQuat **13** (15 mg, 90%) as a white solid and **48** (24 mg, quant) as a colourless oil.

Data for **48**:[43] δ_H (200 MHz, $CDCl_3$) 5.61 (2H, s, C(1)H_2), 7.27–8.14 (9H, m, *Ar*, *Ph*); δ_C (125 MHz, $CDCl_3$) 66.7 (*C*(1)), 127.8, 128.1, 129.0, 129.8, 130.1, 131.2, 133.4, 134.0, 134.2, 134.7 (*Ar*, *Ph*), 164.9 (*O*COAr), 191.7 (*C*(2)); *m*/*z* (CI^+) 275 ($[M+H]^+$, 100%).

*4.4.24. (S)-Phenylethane-1,2-diol (S)-**49***

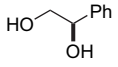


$NaBH_4$ (64 mg, 1.68 mmol) was added to a solution of **21** (100 mg, 0.22 mmol) in MeOH (2 mL) and the resultant solution was stirred for 10 min before concentration in vacuo. The mixture was then partitioned between DCM (2 mL) and 1.0 M aq HCl (2 mL), the organic layer separated and the aqueous layer extracted with DCM (3×5 mL). The combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (eluent EtOAc/40–60 °C petrol, 2:1, and then increased to EtOAc) gave SuperQuat **13** as a white solid (32 mg, 78%) and (*S*)-**49** as a white amorphous solid (24 mg, 81%, >98% ee).

Data for (*S*)-**49**: $[\alpha]_D^{22}$ +64.0 (*c* 0.25, $CHCl_3$) {lit.[26] $[\alpha]_D^{20}$ +60.5 (*c* 1.15, $CHCl_3$)}; δ_H (200 MHz, $CDCl_3$) 2.48 (1H, br s, O*H*), 2.88 (1H, br s, O*H*), 3.67–3.75 (2H, m, C(2)H_2), 4.82 (1H, dd, *J* 7.9, 3.8, C(1)*H*), 7.27–7.38 (5H, m, *Ph*).

The ee of (*S*)-phenylethane-1,2-diol was determined by ChiralGC analysis [flow rate 1.5 mL/min; 40 °C isotherm for 120 min; 4 °C/min ramp to 140 °C; 140 °C isotherm for 120 min; retention times: t_R (*S*)=159.25 min; t_R (*R*)=159.87 min] and comparison with an authentic racemic sample.

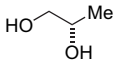
4.4.25. (*R*)-Phenylethane-1,2-diol (*R*)-**49**



$NaBH_4$ (64 mg, 1.68 mmol) was added to a solution of **41** (100 mg, 0.22 mmol) in MeOH (2 mL) and the resultant solution was stirred for 10 min before concentration in vacuo. The mixture was then partitioned between DCM (2 mL) and 1.0 M aq HCl (2 mL), the organic layer separated and the aqueous layer extracted with DCM (3×5 mL). The combined organic layers were dried and concentrated in vacuo. Purification via flash column chromatography (eluent EtOAc/40–60 °C petrol, 2:1, and then increased to EtOAc) gave SuperQuat **13** as a white solid (37 mg, 90%) and (*R*)-**49** as a white amorphous solid (18 mg, 60%, >98% ee).

Data for (*R*)-**49**: $[\alpha]_D^{19}$ −54.1 (*c* 0.9, $CHCl_3$).

4.4.26. (*S*)-Propane-1,2-diol (*S*)-**50**



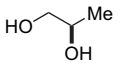
$NaBH_4$ (658 mg, 17.4 mmol) was added to a solution of **23** (900 mg, 2.23 mmol) in MeOH (10 mL) and the resultant solution was stirred for 10 min before concentration in vacuo. H_2O (5 mL) was added and the resultant slurry was filtered through cotton wool, followed by Celite (eluent H_2O). The filtrate was distilled twice and the distillate was dried in a dessicator (over P_2O_5) to give (*S*)-**50** as a colourless oil (61 mg, 37%); $[\alpha]_D^{23}$ +18.1 (*c* 0.15, H_2O) {lit.[27] $[\alpha]_D^{31}$ +20.7 (*c* 7.5, H_2O)}; δ_H (400 MHz, D_2O) 1.01 (3H, d, *J* 6.4, CH_3CHCH$_2$), 3.31 (1H, dd, *J* 6.8, 11.6, CH$_3$CHCH_2), 3.42 (1H, dd, *J* 4.1, 11.6, CH$_3$CHCH_2), 3.70–3.78 (1H, m, CH$_3$C*H*CH$_2$).

The filter cake was washed with $CHCl_3$ (50 mL), the filtrate was dried and concentration in vacuo. Purification via flash column chromatography (eluent EtOAc/40–60 °C petrol, 2:1) gave SuperQuat **13** as a white solid (422 mg, 99%).

(*S*)-Propane-1,2-diol (*S*)-**50** (42 mg, 0.552 mmol) was dissolved in pyridine (0.5 mL), and DMAP (7 mg) and Ac_2O (261 μL) were added sequentially. The reaction mixture was stirred at rt for 24 h, after which it was cooled to 0 °C and H_2O (1 mL) was added. After warming to rt, the mixture was extracted with Et_2O (3×10 mL) and the combined organic extracts were washed sequentially with satd aq $CuSO_4$ (2×20 mL), H_2O (2×20 mL) and satd aq $NaHCO_3$ (20 mL), then dried, and concentrated in vacuo to give (*S*)-propane-1,2-diol diacetate as a colourless oil (35 mg, 40%, >98% ee); $[\alpha]_D^{23}$ −13.0 (*c* 0.8, MeOH) {lit.[44] $[\alpha]_D^{25}$ −14.7 (*c* 0.15, MeOH)}; δ_H (400 MHz, $CDCl_3$) 1.26 (3H, d, *J* 6.5, C(3)H_3), 2.06 (3H, s, CO*Me*), 2.07 (3H, s, CO*Me*), 4.04 (1H, dd, *J* 11.8, 6.6, C(1)H_A), 4.16 (1H, dd, *J* 11.8, 3.5, C(1)H_B), 5.10–5.15 (1H, m, C(2)*H*).

The ee of (*S*)-propane-1,2-diol diacetate was determined by ChiralGC analysis [flow rate 3 mL/min; 70 °C isotherm for 15 min; retention times: t_R (*S*)=13.24 min; t_R (*R*)=14.35 min] and comparison with an authentic racemic sample.

4.4.27. (*R*)-Propane-1,2-diol (*R*)-**50**



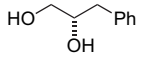
$NaBH_4$ (1.47 g, 38.9 mmol) was added to a solution of **37** (2.02 g, 4.99 mmol) in MeOH (20 mL) and the resultant solution was stirred for 10 min before concentration in vacuo. H_2O (10 mL) was added and the resultant slurry was filtered through cotton wool followed by Celite (eluent H_2O). The filtrate was distilled twice and the distillate dried in a dessicator (over P_2O_5) to give (*R*)-**50** as a colourless oil (151 mg, 40%); $[\alpha]_D^{23}$ −19.6 (*c* 1.6, H_2O).

The filter cake was washed with $CHCl_3$ (50 mL) and the filtrate was dried and concentrated in vacuo. Purification via flash column chromatography (eluent EtOAc/40–60 °C petrol, 2:1) gave SuperQuat **13** as a white solid (861 mg, 90%).

(*R*)-Propane-1,2-diol (*R*)-**50** (20 mg, 0.26 mmol) was dissolved in pyridine (0.5 mL), and DMAP (7 mg) and Ac_2O (124 μL) were added sequentially. The reaction mixture was stirred at rt for 24 h, after which it was cooled to 0 °C and H_2O (1 mL) was added. After warming to rt, the mixture was extracted with Et_2O (3×10 mL) and the combined organic extracts were washed sequentially with satd aq $CuSO_4$ (2×20 mL), H_2O (2×20 mL) and satd aq $NaHCO_3$ (20 mL), then dried, and concentrated in vacuo to give (*R*)-propane-1,2-diol diacetate as a colourless oil (16 mg, 38%, >98% ee); $[\alpha]_D^{19}$ +13.2 (*c* 2.2, MeOH).

The ee of (*R*)-propane-1,2-diol diacetate was determined by ChiralGC analysis [flow rate 3 mL/min; 70 °C isotherm for 15 min; retention times: t_R (*S*)=13.24 min; t_R (*R*)=14.35 min] and comparison with an authentic racemic sample.

4.4.28. (*S*)-3-Phenyl-propane-1,2-diol (*S*)-**51**

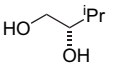


$NaBH_4$ (112 mg, 2.96 mmol) was added to a solution of **25** (177 mg, 0.37 mmol) in MeOH (6 mL) and the resultant solution was stirred for 10 min before concentration in vacuo. The mixture was then partitioned between DCM (2 mL) and 1.0 M aq HCl (2 mL), the organic layer was separated and the aqueous layer was extracted with DCM (3×5 mL). The combined organic layers were dried and concentrated in vacuo. Purification via column chromatography (eluent EtOAc/40–60 °C petrol, 2:1, and then increased to EtOAc) gave SuperQuat **13** as a white solid (70 mg, 99%) and (*S*)-**51** as a white amorphous solid (52 mg, 93%).

Data for (*S*)-**51**: $[\alpha]_D^{24}$ −33.5 (*c* 0.9, EtOH) {lit.[28,45] $[\alpha]_D^{20}$ −36 (*c* 1.0, EtOH)}; δ_H (400 MHz, $CDCl_3$) 2.23 (2H, br s, O*H*), 2.78 (2H, m, C(3)H_2), 3.53 (1H, dd, *J* 11.2, 7.0, C(1)H_A), 3.69 (1H, dd, *J* 11.2, 3.1, C(1)H_B), 3.95 (1H, m, C(2)*H*), 7.20–7.56 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 39.8, 66.0, 73.3, 126.6, 128.6, 129.3, 137.7; *m*/*z* (CI^+) 152 ($[M]^+$, 100%); HRMS (CI^+) found 152.0836, $C_9H_{12}O_2^+$ ($[M]^+$) requires 152.0832.

The ee of (*S*)-3-phenyl-propane-1,2-diol bis-trifluoroacetate was determined by ChiralGC analysis [flow rate 2 mL/min; 50 °C isotherm for 120 min; 4 °C/min ramp to 110 °C; 110 °C isotherm for 60 min; retention times: t_R (*S*)=139.38 min; t_R (*R*)=139.89 min] and comparison with an authentic racemic sample.

4.4.29. (*S*)-3-Methylbutane-1,2-diol (*S*)-**52**



$LiAlH_4$ (75 mg, 1.91 mmol) was added to a solution of **27** (310 mg, 0.72 mmol) in THF (10 mL) and the resultant solution was

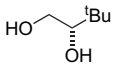
stirred for 1 h before being quenched with satd aq NH_4Cl (1 mL). The mixture was diluted with brine (10 mL), the organic layer was separated and the aqueous layer was extracted with EtOAc (3×10 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 40–60 °C petrol/Et_2O, 3:1, and then increased to Et_2O) gave SuperQuat **13** as a white solid (107 mg, 81%) and (*S*)-**52** as a colourless oil (42 mg, 56%).

Data for (*S*)-**52**: $[\alpha]_D^{25}$ +15.2 (*c* 0.9, $CHCl_3$) {lit.[46] for enantiomer $[\alpha]_D^{20}$ −11.0 (*c* 1.0, $CHCl_3$)}; ν_{max} (film) 3442 (O–H); δ_H (400 MHz, $CDCl_3$) 0.93 (3H, d, *J* 6.8, CH_3CHCH_3), 0.98 (3H, d, *J* 6.8, CH$_3$CHCH_3), 1.72 (1H, octet, *J* 6.8, C(3)*H*), 2.20 (2H, br s, O*H*), 3.44 (1H, ddd, *J* 8.2, 6.8, 2.8, C(2)*H*), 3.52 (1H, dd, *J* 10.8, 8.2, C(1)H_A), 3.72 (1H, dd, *J* 10.8, 2.8, C(1)H_B); δ_C (100 MHz, $CDCl_3$) 18.2, 18.7, 30.9, 63.9, 77.2; *m*/*z* (ESI^+) 122 ($[M+NH_4]^+$, 100%); HRMS (ESI^+) found 122.1183, $C_5H_{16}NO_2^+$ ($[M+NH_4]^+$) requires 122.1176.

Diol (*S*)-**52** (20 mg) was dissolved in pyridine (0.5 mL), and DMAP (2 mg) and Ac_2O (0.1 mL) were added sequentially. The reaction mixture was stirred at rt for 24 h, after which it was cooled to 0 °C and H_2O (1 mL) was added. After warming to rt, the mixture was extracted with Et_2O (3×10 mL) and the combined organic extracts were washed sequentially with satd aq $CuSO_4$ (2×20 mL), H_2O (2×20 mL) and satd aq $NaHCO_3$ (20 mL), then dried, and concentrated in vacuo to give (*S*)-3-methyl-butane-1,2-diol diacetate as a colourless oil (30 mg, 78%, 96% ee); δ_H (400 MHz, $CDCl_3$) 0.94 (3H, d, *J* 2.3, C(3)*Me*$_A$), 0.95 (3H, d, *J* 2.3, C(3)*Me*$_B$), 1.98–1.90 (1H, m, C(3)*H*), 2.06 (3H, s, CO*Me*), 2.11 (3H, s, CO*Me*), 4.06 (1H, dd, *J* 12.0, 7.2, C(1)H_A), 4.28 (1H, dd, *J* 12.0, 3.0, C(1)H_B), 4.91 (1H, dt, *J* 7.2, 3.0, C(2)*H*).

The ee of (*S*)-3-methyl-butane-1,2-diol diacetate was determined by ChiralGC analysis [flow rate 1 mL/min; 40 °C isotherm for 30 min; 5 °C/min ramp to 60 °C; 60 °C isotherm for 30 min; 20 °C/min ramp to 190 °C; 190 °C isotherm for 2 min; retention times: t_R (*S*)=69.41 min; t_R (*R*)=69.45 min] and comparison with an authentic racemic sample.

4.4.30. (*S*)-3,3-Dimethyl-butane-1,2-diol (*S*)-*53*



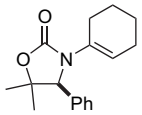
$LiAlH_4$ (90 mg, 2.3 mmol) was added to a solution of **29** (370 mg, 0.83 mmol) in THF (10 mL) and the resultant solution was stirred for 1 h before being quenched with satd aq NH_4Cl (1 mL). The mixture was diluted with brine (10 mL), the organic layer was separated and the aqueous layer was extracted with EtOAc (3×10 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 40–60 °C petrol/Et_2O, 3:1, and then increased to Et_2O) gave SuperQuat **13** as a white solid (133 mg, 84%) and (*S*)-**53** as a colourless oil (50 mg, 51%).

Data for (*S*)-**53**: $[\alpha]_D^{25}$ +31.9 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3279 (O–H); δ_H (400 MHz, $CDCl_3$) 0.90 (9H, s, CMe_3), 2.65 (2H, br s, O*H*), 3.36 (1H, dd, *J* 9.5, 2.6, C(2)*H*), 3.46 (1H, t, *J* 9.5, C(1)H_A), 3.71 (1H, dd, *J* 9.5, 2.6, C(1)H_B); δ_C (100 MHz, $CDCl_3$) 25.9, 33.5, 63.3, 79.6; HRMS (CI^+) found 136.1338, $C_6H_{18}NO_2^+$ ($[M+NH_4]^+$) requires 136.1332.

Diol (*S*)-**53** (20 mg) was dissolved in pyridine (0.5 mL), and DMAP (2 mg) and Ac_2O (0.1 mL) were added sequentially. The reaction mixture was stirred at rt for 24 h, after which it was cooled to 0 °C and H_2O (1 mL) added. After warming to rt, the mixture was extracted with Et_2O (3×10 mL) and the combined organic extracts were washed sequentially with satd aq $CuSO_4$ (2×20 mL), H_2O (2×20 mL) and satd aq $NaHCO_3$ (20 mL), then dried and concentrated in vacuo to give (*S*)-3,3-dimethyl-butane-1,2-diol diacetate as a colourless oil (22 mg, 65%, 96% ee); δ_H (400 MHz, $CDCl_3$) 0.95 (9H, s, CMe_3), 2.02 (3H, s, CO*Me*), 2.09 (3H, s, CO*Me*), 4.00 (1H, dd, *J* 11.7, 9.0, C(1)H_A), 4.95 (1H, dd, *J* 9.0, 2.4, C(2)*H*), 4.38 (1H, dd, *J* 11.7, 2.4, C(1)H_B).

The ee of (*S*)-3,3-dimethyl-butane-1,2-diol diacetate was determined by ChiralGC analysis [flow rate 1 mL/min; 40 °C isotherm for 30 min; 5 °C/min ramp to 60 °C; 60 °C isotherm for 30 min; 20 °C/min ramp to 190 °C; 190 °C isotherm for 2 min; retention times: t_R (*R*)=51.00 min; t_R (*S*)=51.07 min] and comparison with an authentic racemic sample.

4.4.31. (*S*)-N(3)-(Cyclohex-1′-en-1′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one *54*



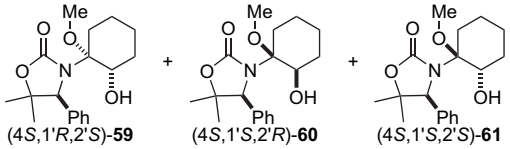
Following *General Procedure 1*, TsOH (ca. 100 mg), cyclohexanone (7.70 g, 78.6 mmol) and **13** (5.0 g, 26.2 mmol) in PhMe (120 mL) gave the crude reaction mixture. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 3:1) gave **54** as a white solid (4.48 g, 63%). Found C, 75.2; H, 8.0; N, 4.9%. $C_{17}H_{21}NO_2$ requires C, 75.25; H, 7.8; N, 4.9%. Mp 110–112 °C (Et_2O); $[\alpha]_D^{24}$ +36.6 (*c* 0.8, $CHCl_3$); ν_{max} (KBr) 1725; δ_H (400 MHz, $CDCl_3$) 0.96 (3H, s, C(5)*Me*$_A$), 1.41–1.65 (4H, m, C(4′)H_A, C(5′)H_A, C(6′)H_2), overlapping 1.59 (3H, s, C(5)*Me*$_B$), 1.96–2.02 (2H, m, C(3′)H_2), 2.23–2.28 (1H, m, C(4′)H_B), 2.29–2.38 (1H, m, C(5′)H_B), 4.67 (1H, s, C(4)*H*), 5.44 (1H, app dq, *J* 3.7, 2.0, C(2′)*H*), 7.26 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 21.6, 22.5, 23.0, 24.2, 26.4, 28.6, 70.0, 80.7, 117.9, 127.4, 127.5, 128.0, 133.6, 136.3, 155.5.

4.4.31.1. *X-ray crystal structure determination for **54***.

Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

X-ray crystal structure data for **54** [$C_{17}H_{21}NO_2$]: *M*=271.36, orthorhombic, space group *Pbca*, *a*=9.9633(1) Å, *b*=10.7233(1) Å, *c*=26.7595(4) Å, *V*=2858.97(6) Å^3, *Z*=8, μ=0.082 mm^{-1}, colourless block, crystal dimensions=0.2×0.2×0.2 mm^3. A total of 3149 unique reflections were measured for $5<\theta<27$ and 2502 reflections were used in the refinement. The final parameters were wR_2=0.049 and R_1=0.039 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653138. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.4.32. (4*S*,1′*R*,2′*S*)-, (4*S*,1′*S*,2′*R*)- and (4*S*,1′*S*,2′*S*)-N(3)-(1′-Methoxy-2′-hydroxy-cyclohex-1′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one (4*S*,1′*R*,2′*S*)-*59*, (4*S*,1′*S*,2′*R*)-*60* and (4*S*,1′*S*,2′*S*)-*61*



A solution of *m*CPBA (1.27 g, 7.37 mmol) in MeOH (10 mL) was dried over Na_2SO_4 and subsequently added to a solution of **54**

(500 mg, 1.84 mmol) in MeOH (10 mL) at −20 °C. After stirring for 4 h, DCM was added (20 mL) and the organic layer was washed successively with satd aq Na_2CO_3 (5×20 mL) and brine (20 mL), then dried over Na_2SO_4 and concentrated in vacuo to give a 67:30:2:1 mixture of **59**/**60**/**61**/**62**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 4:1) gave **61** as a white solid (first to elute, 125 mg, 11%), **60** as a colourless oil (second to elute, 314 mg, 26%) and **59** as a white solid (third to elute, 590 mg, 50%).

Data for **59**: mp 160–162 °C (Et_2O); $[\alpha]_D^{24}$ −99.7 (*c* 1.3, $CHCl_3$); ν_{max} (KBr) 3433 (O–H), 1727 (C=O); δ_H (400 MHz, C_6D_6) 0.81 (3H, s, C(5)*Me*$_A$), 1.01–1.11 (1H, m, C(4′)*H*$_A$), 1.22–1.34 (2H, m, C(5′)*H*$_2$), 1.35–1.41 (1H, m, C(6′)*H*$_A$), 1.41 (3H, s, C(5)*Me*$_B$), 1.51–1.61 (1H, m, C(4′)*H*$_B$), 1.73–1.87 (2H, m, C(3′)*H*$_2$), 2.16–2.25 (1H, m, C(6′)*H*$_B$), 3.28 (3H, s, O*Me*), 3.56 (1H, br s, O*H*), 4.08–4.17 (1H, m, C(2′)*H*), 4.40 (1H, s, C(4)*H*), 6.77–7.49 (5H, m, *Ph*); δ_C (100 MHz, C_6D_6) 22.2, 23.5, 23.7, 29.1, 31.4, 32.6, 51.4, 67.8, 73.2, 80.7, 91.6, 128.1, 128.2, 128.4, 140.1, 157.8; *m*/*z* (ESI$^+$) 661 ([2M+Na]$^+$, 100%), 342 ([M+Na]$^+$, 53%); HRMS (ESI$^+$) found 342.1678, $C_{18}H_{25}NNaO_4^+$ ([M+Na]$^+$) requires 342.1676.

Data for **60**: $[\alpha]_D^{20}$ +24.1 (*c* 0.7, $CHCl_3$), ν_{max} (film) 3411 (O–H), 1721 (C=O); δ_H (400 MHz, C_6D_6) 0.65 (3H, s, C(5)*Me*$_A$), 0.79–0.92 (1H, m, C(4′)*H*$_A$), 1.06–1.18 (2H, m, C(5′)*H*$_2$), 1.29 (3H, s, C(5)*Me*$_B$), 1.32–1.42 (1H, m, C(4′)*H*$_B$), 1.68–1.79 (4H, m, C(3′)*H*$_2$, C(6′)*H*$_2$), 3.09 (3H, s, O*Me*), 3.88–3.97 (1H, m, C(2′)*H*), 4.09 (1H, br s, O*H*), 4.22 (1H, s, C(4)*H*), 6.99–7.46 (5H, m, *Ph*); δ_C (100 MHz, C_6D_6) 22.3, 23.4, 24.0, 29.1, 31.7, 32.1, 50.9, 68.6, 74.7, 80.6, 91.2, 128.1, 128.2, 128.4, 139.5, 157.7; *m*/*z* (ESI$^+$) 378 ([M+59]$^+$, 100%); HRMS (ESI$^+$) found 320.1861, $C_{18}H_{26}NO_4^+$ ([M+H]$^+$) requires 320.1856.

Data for **61**: found C, 67.65; H, 7.9; N, 4.4%. $C_{18}H_{25}NO_4$ requires C, 67.7; H, 7.9; N, 4.4%. Mp 142–144 °C (Et_2O); $[\alpha]_D^{24}$ +105.5 (*c* 1.0, $CHCl_3$); ν_{max} (KBr) 3391 (O–H), 1703 (C=O); δ_H (400 MHz, C_6D_6) 0.62 (3H, s, C(5)*Me*$_A$), 1.15–1.23 (2H, m, C(4′)*H*$_A$, C(5′)*H*$_A$), 1.28 (3H, s, C(5)*Me*$_B$), 1.37–1.46 (1H, m, C(5′)*H*$_B$), 1.43–1.53 (1H, m, C(6′)*H*$_A$), 1.50–1.56 (1H, m, C(3′)*H*$_A$), 1.63–1.72 (2H, m, C(4′)*H*$_B$, C(6′)*H*$_B$,), 1.84–1.87 (1H, m, C(3′)*H*$_B$), 3.07 (3H, s, O*Me*), 4.16 (1H, d, *J* 3.0, O*H*), 4.33 (1H, s, C(4)*H*), 4.97 (1H, s, C(2′)*H*), 6.98–7.31 (5H, m, *Ph*); δ_C (100 MHz, C_6D_6) 19.3, 22.4, 24.4, 29.5, 29.6, 33.2, 49.7, 65.3, 67.0, 81.2, 92.6, 128.1, 128.3, 128.5, 140.5, 158.6; *m*/*z* (ESI$^+$) 378 ([M+59]$^+$, 100%); HRMS (ESI$^+$) found 342.1680, $C_{18}H_{25}NNaO_4^+$ ([M+Na]$^+$) requires 342.1676.

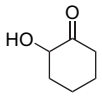
*4.4.32.1. X-ray crystal structure determination for **59**.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

X-ray crystal structure data for **59** [$C_{18}H_{25}NO_4$]: *M*=638.80, orthorhombic, space group $P2_12_12_1$, *a*=9.7982(2) Å, *b*=13.8669(2) Å, *c*=25.6927(6) Å, *V*=3490.88(12) Å^3, *Z*=8, μ=0.085 mm^{-1}, colourless block, crystal dimensions=0.1×0.1×0.1 mm^3. A total of 4385 unique reflections were measured for 5<θ<27 and 3569 reflections were used in the refinement. The final parameters were wR_2=0.057 and R_1=0.051 [$I>1.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 661684. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

*4.4.32.2. X-ray crystal structure determination for **61**.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

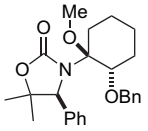
X-ray crystal structure data for **61** [$C_{18}H_{25}NO_4$]: *M*=319.40, tetragonal, space group $P4_1$, *a*=12.8576(3) Å, *b*=12.8576(3) Å, *c*=10.3348(3) Å, *V*=1708.53(7) Å^3, *Z*=4, μ=0.087 mm^{-1}, colourless block, crystal dimensions=0.2×0.2×0.2 mm^3. A total of 2052 unique reflections were measured for 5<θ<27 and 1711 reflections were used in the refinement. The final parameters were wR_2=0.045 and R_1=0.039 [$I>2.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653140. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

*4.4.33. 2-Hydroxy-cyclohexanone **63***



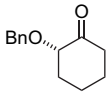
Aq HCl (10%, 2 mL) was added to a solution of **59** (200 mg, 0.63 mmol) in THF (2 mL) at 0 °C. The reaction mixture was allowed to warm to rt over 12 h after which it was neutralised with satd aq Na_2CO_3 (3 mL) and the aqueous phase was extracted with EtOAc (3×10 mL). The combined organic extracts were then washed with brine, dried over Na_2SO_4 and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 1:1) gave **63** as a colourless oil (39 mg, 55%); $[\alpha]_D^{20}$ −1.5 (*c* 1.0, $CHCl_3$) {lit.[31] for 90% ee $[\alpha]_D^{20}$ −13.3 (*c* 0.5, $CHCl_3$); lit.[32] for enantiomer, 96% ee $[\alpha]_D^{18}$ +23.3 (*c* 0.6, $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.45–1.76 (3H, m, C(3)*H*$_A$, C(4)*H*$_A$, C(5)*H*$_A$), 1.83–1.92 (1H, m, C(4)*H*$_B$), 2.06–2.15 (1H, m, C(5)*H*$_B$), 2.32–2.37 (1H, m, C(6)*H*$_A$), 2.41–2.49 (1H, m, C(3)*H*$_B$), 2.52–2.61 (1H, m, C(6)*H*$_B$), 3.63 (1H, br s, O*H*), 4.12 (1H, ddd, *J* 12.1, 6.6, 1.7, C(2)*H*).

*4.4.34. (4S,1′S,2′S)-N(3)-(1′-Methoxy-2′-benzyloxy-cyclohex-1′-yl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one **65***



NaH (60% dispersion in mineral oil, 26 mg, 0.64 mmol) and BnBr (145 mg, 0.85 mmol) were sequentially added to a solution of **61** (135 mg, 0.42 mmol) in DMF (5 mL) at 0 °C. The reaction mixture was allowed to warm to rt and stirred for a further 6 h, after which H_2O was added and the aqueous phase was extracted with EtOAc (2×10 mL). The combined organic extracts were washed with satd aq Na_2CO_3 solution and brine, then dried over Na_2SO_4 and concentrated in vacuo. Purification via flash column chromatography (silica, 30–40 °C petrol/Et_2O, 4:1) gave **65** as a white solid (165 mg, 95%). Found C, 73.1; H, 7.6; N, 3.4%. $C_{25}H_{31}NO_4$ requires C, 73.3; H, 7.6; N, 3.4%. Mp 134 °C (Et_2O); $[\alpha]_D^{23}$ +41.5 (*c* 0.9, $CHCl_3$); ν_{max} (KBr) 1733 (C=O); δ_H (400 MHz, C_6D_6) 0.63 (3H, s, C(5)Me$_A$), 1.10–1.19 (1H, m, C(4′)*H*$_A$), 1.32–1.42 (1H, m, C(6′)*H*$_A$), 1.24 (3H, s, C(5)*Me*$_B$), 1.63–1.78 (3H, m, C(4′)*H*$_B$, C(5′)*H*$_A$), 1.79–1.92 (2H, m, C(3′)*H*$_2$), 2.57–2.63 (1H, m, C(6′)*H*$_B$), 3.23 (3H, s, O*Me*), 4.26 (1H, s, C(4)*H*), 4.45 (1H, d, *J* 10.7, OC*H*$_A$H$_B$Ph), 4.53 (1H, d, *J* 10.7, OCH$_A$*H*$_B$Ph), 4.80 (1H, br s, C(2′)*H*), 6.49–7.48 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.1, 22.7, 23.9, 26.5, 29.3, 34.1, 51.8, 68.1, 71.7, 80.1, 80.2, 90.4, 127.2, 127.7, 127.8, 128.0, 128.4, 139.3, 139.8, 155.5.

*4.4.35. (S)-2-Benzyloxycyclohexanone (S)-**66***

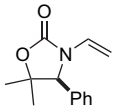


*From **59***. NaH (60% dispersion in mineral oil, 15 mg, 0.38 mmol) and BnBr (63.9 mg, 0.38 mmol) were sequentially added to a solution of **59** (100 mg, 0.31 mmol) in DMF (2 mL) at 0 °C and the reaction mixture was allowed to warm to rt. After stirring for a further 10 h, H_2O was added and the aqueous phase was extracted with EtOAc (2×6 mL), the combined organic extracts were washed with satd aq Na_2CO_3 (10 mL) and brine (10 mL), then dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 9:1) gave (*S*)-**66** as a colourless oil (5.8 mg, 9%).

*From **65***. Aq HCl (10%, 2 mL) was added to a solution of **65** (100 mg, 0.24 mmol) in THF (2 mL) at 0 °C. The reaction mixture was allowed to warm to rt over 12 h, after which time satd aq Na_2CO_3 (5 mL) was added and the aqueous phase was extracted with EtOAc (3×5 mL). The combined organic extracts were washed with brine (10 mL), dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 9:1) gave (*S*)-**66** as a colourless oil (44 mg, 69%).

Data for (*S*)-**66**: $[\alpha]_D^{23}$ −103.0 (*c* 0.8, $CHCl_3$) {lit.[34] $[\alpha]_D^{21}$ −108.1 (*c* 1.2, $CHCl_3$)}; ν_{max} (film) 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 1.54–1.75 (2H, m, C(4)H_A, C(5)H_A), 1.81–1.88 (1H, m, C(3)H_A), 1.90–1.99 (2H, m, C(4)H_B, C(5)H_B), 2.17–2.22 (1H, m, C(3)H_B), 2.23–2.31 (1H, m, C(6)H_A), 2.51–2.59 (1H, m, C(6)H_B), 3.83–3.92 (1H, m, C(2)*H*), 4.49 (1H, d, *J* 12.0, OCH_A) 4.79 (1H, d, *J* 12.0, OCH_B), 7.28–7.40 (5H, m, *Ph*); *m*/*z* (ESI^+) 205 ($[M+H]^+$, 100%); HRMS (ESI^+) found 205.1223, $C_{13}H_{17}O_2^+$ ($[M+H]^+$) requires 205.1223.

*4.4.36. (S)-N(3)-Ethenyl-4-phenyl-5,5-dimethyl-oxazolidin-2-one **72***



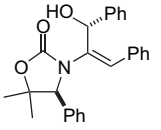
Preparation of (DPP)Pd(OCOCF$_3$)$_2$. A solution of $Pd(OCOCF_3)_2$ (100 mg, 0.30 mmol) in PhMe (2 mL) was added to a solution of DPP[†] (100 mg, 0.30 mmol) in PhMe (2 mL) and stirred at rt for 12 h. The resultant slurry was filtered to give (DPP)$Pd(OCOCF_3)_2$ as a pale brown solid (180 mg, 90%) that was used without purification.

(DPP)$Pd(OCOCF_3)_2$ (100 mg, 0.15 mmol) was added to a solution of **13** (500 mg, 2.62 mmol) in butyl vinyl ether (3.4 mL, 26.2 mmol) and the reaction mixture was stirred at 76 °C for 6 h after which time an additional portion of (DPP)$Pd(OCOCF_3)_2$ (25 mg, 0.38 mmol) and butyl vinyl ether (3.4 mL, 26.2 mmol) were added to the reaction mixture. Stirring was continued for a further 6 h at 76 °C before the mixture was allowed to cool to rt, filtered and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 9:1) gave **72** as a white solid (362 mg, 64%). Found C, 71.9; H, 7.0; N, 6.45%. $C_{17}H_{21}NO_2$ requires C, 71.8; H, 7.0; N, 6.5%. Mp 135 °C (Et_2O); $[\alpha]_D^{23}$ +85.0 (*c* 0.8, $CHCl_3$); ν_{max} (KBr) 1749; δ_H (400 MHz, $CDCl_3$) 0.95 (3H, s, C(5)Me_A), 1.60 (3H, s, C(5)Me_B), 3.96 (1H, d, *J* 16.0, C(2′)H_A), 4.29 (1H, d, *J* 9.3, C(2′)H_B), 4.63 (1H, s, C(4)*H*), 6.90 (1H, dd, *J* 16.0, 9.3, C(1′)*H*), 7.11–7.41 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.8, 29.3, 67.7, 82.2, 95.6, 128.6, 128.7, 128.9, 134.8, 154.8; *m*/*z* (ESI^+) 276 ($[M+59]^+$, 45%); HRMS (FI^+) found 217.1107, $C_{13}H_{15}NO_2^+$ ($[M]^+$) requires 217.1097.

*4.4.36.1. X-ray crystal structure determination for **72***. Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

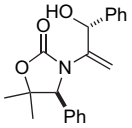
X-ray crystal structure data for **72** [$C_{13}H_{15}NO_2$]: *M*=217.27, orthorhombic, space group $P2_12_12_1$, *a*=8.21470(10) Å, *b*=11.4424(2) Å, *c*=12.7093(3) Å, *V*=1194.62(4) Å^3, *Z*=4, μ=0.082 mm^{-1}, colourless block, crystal dimensions=0.2×0.2×0.2 mm^3. A total of 1570 unique reflections were measured for $5<\theta<27$ and 1173 reflections were used in the refinement. The final parameters were wR_2=0.52 and R_1=0.047 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653141. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

*4.4.37. (4S,1″R,E)-3-[1′-(1″-Hydroxy-1″-phenyl-methyl)-2′-phenyl-ethenyl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one **75***



^{t}BuLi (1.7 M in pentane, 0.8 mL, 1.36 mmol) was added dropwise via syringe to a solution of **14** (200 mg, 0.68 mmol) in THF (20 mL) at −78 °C and stirred for 45 min before the addition of PhCHO (144 mg, 1.36 mmol). The reaction mixture was stirred at −78 °C for a further 2 h before being allowed to warm to rt over a further 12 h. The reaction mixture was quenched with satd aq NH_4Cl (5 mL) and diluted with H_2O (20 mL). The mixture was extracted with EtOAc (5×20 mL), the combined organic extracts were dried and concentrated in vacuo to give a 92.5:7.5 mixture of **75**/**76**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 5:1) gave **75** as a white solid (162 mg, 60%, >98% de); mp 149 °C (Et_2O); $[\alpha]_D^{23}$ −222.9 (*c* 0.3, $CHCl_3$); ν_{max} (KBr) 3393 (O–H), 1710 (C=O); δ_H (400 MHz, $CDCl_3$), 0.83 (3H, s, C(5)Me_A), 0.90 (3H, s, C(5)Me_B), 4.79 (1H, s, C(4)*H*), 5.85 (1H, d, *J* 10.6, C(1″)*H*), 6.04 (1H, d, *J* 10.6, O*H*), 6.22 (1H, s, C(2′)*H*), 7.17–7.44 (15H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 23.6, 27.7, 71.5, 73.0, 83.3, 124.6 125.5, 126.8, 127.1, 127.7, 128.2, 128.4, 128.9, 129.2, 134.9, 136.8, 138.4, 141.5, 157.3; *m*/*z* (ESI^+) 400 ($[M+H]^+$, 100%); HRMS (ESI^+) found 400.1916, $C_{26}H_{26}NO_3^+$ ($[M+H]^+$) requires 400.1907.

*4.4.38. (4S,1″R)-3-[(1″-Hydroxy-1″-phenyl-methyl)]ethenyl-4-phenyl-5,5-dimethyl-oxazolidin-2-one **77***



^{t}BuLi (1.7 M in pentane, 0.5 mL, 0.83 mmol) was added dropwise via syringe to a solution of **72** (90 mg, 0.41 mmol) in THF (5 mL) at −78 °C and stirred for 45 min before the addition of PhCHO (97 mg, 0.91 mmol). The reaction mixture was stirred at −78 °C for a further 2 h before being allowed to warm to rt over a further 12 h. The reaction mixture was quenched with satd aq

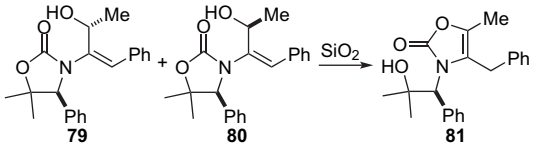
[†] DPP=4,7-diphenyl-1,10-phenanthroline.

NH_4Cl (1 mL) and diluted with H_2O (10 mL). The mixture was extracted with EtOAc (5×10 mL) and the combined organic extracts were dried and concentrated in vacuo to give a 67:33 mixture of **77**/**78**. Purification via flash column chromatography (eluent PhMe/acetone, 100:1, and then increased to PhMe/acetone, 10:1) gave a 67:33 mixture of **77**/**78** as a colourless oil (80 mg, 60%).

Selected peaks for **77**: δ_H (400 MHz, $CDCl_3$), 0.86 (3H, s, C(5)Me_A), 1.28 (3H, s, C(5)Me_B), 4.52 (2H, d, *J* 2.2, C(3′)H_2), 4.83 (1H, s, C(4)*H*), 4.99 (1H, d, *J* 7.8, O*H*), 5.63 (1H, d, *J* 7.8, C(1′)*H*); δ_C (100 MHz $CDCl_3$) 23.6, 28.1, 71.6, 74.8, 82.6, 105.3, 135.4, 140.9, 144.8, 156.0.

Selected peaks for **78**: δ_H (400 MHz, $CDCl_3$), 0.85 (3H, s, C(5)Me_A), 1.32 (3H, s, C(5)Me_B), 4.83 (1H, s, C(4)*H*), 4.60 (1H, d, *J* 7.0, O*H*), 4.66 (1H, s, C(3′)H_A), 4.73 (1H, s, C(3′)H_B), 5.72 (1H, d, *J* 7.0, C(1′)*H*); δ_C (100 MHz, $CDCl_3$) 23.8, 28.2, 70.9, 74.3, 82.4, 105.3, 135.0, 140.6, 144.6, 155.8.

*4.4.39. (4S,1″R,E)- and (4S,1″S,E)-N(3)-[1′-(1″-Hydroxy-ethyl)-2′-phenyl-ethenyl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one (4S,1″R,E)-**79** and (4S,1″S,E)-**80**, and (S)-N(3)-(1′-phenyl-2′-hydroxy-2′-methyl-propyl)-4-benzoyl-5-methyl-oxazolid-4-en-2-one **81***



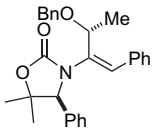
^{t}BuLi (1.7 M in pentane, 0.8 mL, 1.36 mmol) was added dropwise via syringe to a solution of **14** (200 mg, 0.68 mmol) in THF (20 mL) at −78 °C and stirred for 45 min before the addition of MeCHO (60 μL, 1.36 mmol). The reaction mixture was stirred at −78 °C for a further 2 h before being allowed to warm to rt over a further 12 h. The reaction mixture was quenched with satd aq NH_4Cl (5 mL) and diluted with H_2O (20 mL). The mixture was extracted with EtOAc (5×20 mL), the combined organic extracts were dried and concentrated in vacuo to give an 83:17 mixture of **79**/**80**. Filtration through silica (eluent 30–40 °C petrol/Et_2O, 5:1) gave an 83:17 mixture of **79**/**80** as colourless oil (156 mg, 57%); ν_{max} (film) 3416 (O–H), 1736 (C=O); *m*/*z* (ESI$^+$) 360 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) found 338.1753, $C_{21}H_{24}NO_3^+$ ([M+H]$^+$) requires 338.1751.

Data for **79**: δ_H (400 MHz, $CDCl_3$) 1.27 (3H, s, C(5)Me_A), 1.42 (3H, d, *J* 6.3, C(2″)H_3), 1.55 (3H, s, C(5)Me_B), 4.41 (1H, s, C(4)*H*), 5.58–5.63 (1H, m, C(1″)*H*), 5.80 (1H, s, C(2′)*H*), 7.09–7.52 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.6, 28.2, 29.1, 67.8, 71.8, 75.6, 101.6, 126.7, 126.7, 127.9, 128.0, 128.3, 128.8, 129.5, 136.4, 141.5, 158.4.

Data for **80**: δ_H (400 MHz, $CDCl_3$) 0.99 (3H, s, C(5)Me_A), 1.19 (3H, d, *J* 6.3, C(2″)H_3), 1.26 (3H, s, C(5)Me_B), 4.41 (1H, s, C(4)*H*), 5.77–5.82 (1H, m, C(1″)*H*), 5.90 (1H, s, *C*(2′)*H*), 7.09–7.52 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.8, 27.9, 29.0, 67.8, 71.1, 75.9, 101.6, 127.6, 128.0, 128.1, 128.2, 128.8, 129.2, 136.0, 137.9, 157.2.

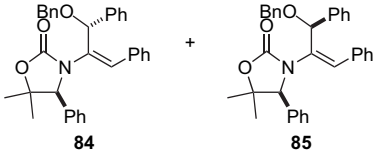
Attempted further purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 5:1) gave **81** as a colourless oil (156 mg, quant); $[\alpha]_D^{23}$ −149.8 (*c* 1.3, $CHCl_3$); ν_{max} (film) 3381 (O–H), 1734 (C=O); δ_H (400 MHz, $CDCl_3$), 0.87 (3H, s, C(2′)Me_A), 0.99 (3H, s, C(2′)Me_B), 2.13 (3H, s, C(5)*Me*), 3.41 (1H, d, *J* 16.9, CH_AH$_B$Ph), 3.78 (1H, d, *J* 16.9, CH$_A$$H_B$Ph), 4.20 (1H, s, C(1′)*H*), 5.91 (1H, br s, O*H*), 7.18–7.41 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 10.1, 27.9, 28.3, 28.9, 68.0, 71.1, 121.2, 127.6, 128.0, 128.1, 128.3, 128.8, 129.2, 134.9, 136.0, 138.0, 157.2; *m*/*z* (ESI$^+$) 360 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) found 338.1758, $C_{21}H_{24}NO_3^+$ ([M+H]$^+$) requires 338.1751.

*4.4.40. (4S,1″R,E)-N(3)-(1′-(1″-Benzyloxy-ethyl)-2′-phenyl-ethenyl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one **82***



Following *General Procedure 3*, **14** (200 mg, 0.68 mmol), ^{t}BuLi (1.7 M in pentane, 0.8 mL, 1.36 mmol), MeCHO (84 μL, 1.50 mmol) and BnBr (0.16 mL, 1.36 mmol) in THF (20 mL) gave an 83:17 mixture of **82**/**83**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 4:1) gave **82** as a colourless oil (148 mg, 51%, >98% de); $[\alpha]_D^{21}$ +48.8 (*c* 0.8, $CHCl_3$); ν_{max} (film) 1749; δ_H (400 MHz, $CDCl_3$) 0.96 (3H, s, C(5)Me_A), 1.19 (3H, d, *J* 5.0, C(4′)H_3), 1.58 (3H, s, C(5)Me_B), 4.26 (1H, d, *J* 11.5, OCH_A), 4.51 (1H, q, *J* 7.0, C(3′)*H*), 4.60 (1H, d, *J* 11.5, OCH_B), 5.13 (1H, s, C(4)*H*), 7.01–7.45 (16H, m, C(1′)*H*, *Ph*); δ_C (100 MHz, $CDCl_3$) 21.9, 24.2, 28.8, 69.7, 70.9, 71.3, 81.0, 125.4, 126.5, 127.4, 127.6, 128.2, 128.4, 128.6, 128.7, 128.9, 132.1, 134.9, 135.7, 136.3, 137.8, 156.6; *m*/*z* (ESI$^+$) 877 ([2M+Na]$^+$, 100%), 450 (87); HRMS (ESI$^+$) found 450.2044, $C_{28}H_{29}NNaO_3^+$ ([M+Na]$^+$) requires 450.2040.

*4.4.41. (4S,1″R,E)- and (4S,1″S,E)-N(3)-[1′-(1″-Benzyloxy-1″phenyl-methyl)-2′-phenyl-ethenyl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one (4S,1″R,E)-**84** and (4S,1″S,E)-**85***



Following *General Procedure 3*, **14** (200 mg, 0.68 mmol), ^{t}BuLi (1.7 M, 0.8 mL, 1.36 mmol), PhCHO (0.16 mL, 1.50 mmol) and BnBr (0.16 mL, 1.36 mmol) in THF (20 mL) gave a 92:8 mixture of **84**/**85**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 4:1) gave **84** as a white solid (first to elute, 279 mg, 83%, >98% de) and a 17:83 mixture of **84**/**85** as a colourless oil (second to elute, 24 mg, 7%).

Data for **84**: mp 45 °C (Et_2O); $[\alpha]_D^{23}$ +24.3 (*c* 1.6, $CHCl_3$); ν_{max} (KBr) 1748; δ_H (400 MHz, $CDCl_3$) 0.83 (3H, s, C(5)Me_A), 1.47 (3H, s, C(5)Me_B), 4.32 (1H, s, C(4)*H*), 4.52 (1H, d, *J* 11.6, OCH_A), 4.94 (1H, d, *J* 11.6, OCH_B), 5.65 (1H, s, C(3′)*H*), 7.03–7.51 (21H, m, C(1′)*H*, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.1, 28.8, 69.1, 71.2, 74.5, 81.3, 125.4, 125.6, 127.4, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 132.7, 134.6, 136.3, 137.6, 139.1, 156.9; *m*/*z* (ESI$^+$) 548 ([M+59]$^+$, 100%); HRMS (FI$^+$) found 489.2319, $C_{33}H_{31}NO_3^+$ ([M]$^+$) requires 489.2298.

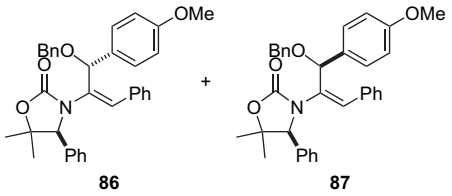
Data for **85**: δ_H (400 MHz, $CDCl_3$) 0.75 (3H, s, C(5)Me_A), 0.81 (3H, s, C(5)Me_B), 3.61 (1H, d, *J* 12.4, OCH_A), 3.81 (1H, d, *J* 12.4, OCH_B), 4.86 (1H, s, C(4)*H*), 5.67 (1H, s, C(3′)*H*), 7.01–7.68 (21H, m, C(1′)*H*, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.0, 27.9, 69.3, 69.9, 74.4, 81.2, 125.5, 126.1, 127.4, 127.6, 127.7, 127.9, 128.1, 128.4, 128.5, 128.6, 131.8, 134.5, 137.3, 137.4, 139.3, 157.0.

*4.4.41.1. X-ray crystal structure determination for **84**.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

X-ray crystal structure data for **84** [$C_{33}H_{31}NO_3$]: *M*=489.61, trigonal, space group $P3_1$, *a*=9.6347(2) Å, *b*=9.6347(2) Å, *c*=24.8494(5) Å, *V*=1997.67(7) Å^3, *Z*=3, μ=0.077 mm^{-1}, colourless

block, crystal dimensions=0.2×0.2×0.2 mm. A total of 2941 unique reflections were measured for $5<\theta<27$ and 2184 reflections were used in the refinement. The final parameters were wR_2=0.036 and R_1=0.036 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653142. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

*4.4.42. (4S,1″R,E)- and (4S,1″S,E)-N(3)-[1′-(1″-Benzyloxy-1″-p-methoxyphenyl-methyl)-2′-phenyl-ethenyl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one (4S,1″R,E)-**86** and (4S,1″S,E)-**87***



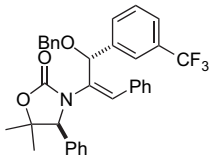
86 **87**

Following *General Procedure 3*, **14** (200 mg, 0.68 mmol), ^{t}BuLi (1.7 M in pentane, 0.8 mL, 1.36 mmol), *p*-anisaldehyde (0.16 mL, 1.50 mmol) and BnBr (0.16 mL, 1.36 mmol) in THF (20 mL) gave a 78:22 mixture of **86**/**87**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 9:1) gave **86** as a colourless oil (first to elute, 353 mg, 72%, >98% de) and **87** as a colourless oil (second to elute, 25 mg, 7%, >98% de).

Data for **86**: $[\alpha]_D^{23}$ +178.9 (*c* 0.8, $CHCl_3$); ν_{max} (film) 1748 (C=O); δ_H (400 MHz, $CDCl_3$) 0.80 (3H, s, C(5)*Me*$_A$), 1.43 (3H, s, C(5)*Me*$_B$), 3.77 (3H, s, O*Me*), 4.37 (1H, s, C(4)*H*), 4.47 (1H, d, *J* 11.6, OC*H*$_A$), 4.87 (1H, d, *J* 11.6, OC*H*$_B$), 5.54 (1H, s, C(3′)*H*), 6.61 (2H, d, *J* 8.7, *Ar*), 7.09 (2H, d, *J* 8.7, *Ar*), 7.10–7.44 (16H, m, C(1′)*H*, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.1, 28.7, 55.3, 69.1, 71.2, 74.3, 81.2, 113.5, 126.7, 127.6, 127.7, 127.9, 128.1, 128.2, 128.3, 128.4, 128.6, 130.9, 132.7, 136.5, 137.6, 156.8, 158.7; *m*/*z* (ESI$^+$) 578 ([M+59]$^+$, 100%); HRMS (FI$^+$) found 519.2426, $C_{34}H_{33}NO_4^+$ ([M]$^+$) requires 519.2404.

Data for **87**: $[\alpha]_D^{23}$ −191.1 (*c* 0.9, $CHCl_3$); ν_{max} (film) 1748 (C=O); δ_H (400 MHz, $CDCl_3$) 0.82 (3H, s, C(5)*Me*$_A$), 0.85 (3H, s, C(5)*Me*$_B$), 3.60 (1H, d, *J* 12.3, OC*H*$_A$), 3.80 (1H, d, *J* 12.3, OC*H*$_B$), 3.84 (3H, s, O*Me*), 4.91 (1H, s, C(4)*H*), 5.59 (1H, s, C(3′)*H*), 6.71 (2H, d, *J* 6.9, *Ar*), 7.06–7.44 (18H, m, C(1′)*H*, *Ar*, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.0, 28.1, 55.4, 69.3, 69.9, 74.3, 81.2, 113.9, 127.3, 127.5, 128.7, 128.9, 128.1, 128.2, 128.4, 128.6, 128.7, 134.6, 131.2, 131.6, 135.2, 137.3, 137.4, 156.8, 159.2; *m*/*z* (ESI$^+$) 578 ([M+59]$^+$, 100%); HRMS (FI$^+$) found 542.2295, $C_{34}H_{33}NNaO_4^+$ ([M+Na]$^+$) requires 542.2302.

*4.4.43. (4S,1″R,E)-N(3)-[1′-(1″-Benzyloxy-1″-m-trifluoromethyl-phenyl-methyl)-2″-phenyl-ethenyl]-4-phenyl-5,5-dimethyl-oxazolidin-2-one **88***

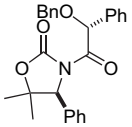


Following *General Procedure 3*, **14** (200 mg, 0.68 mmol), ^{t}BuLi (1.7 M in pentane, 0.8 mL, 1.36 mmol), *m*-trifluoromethyl-benzaldehyde (0.16 mL, 1.50 mmol) and BnBr (0.16 mL, 1.36 mmol) in THF (10 mL) gave a 94:6 mixture of **88**/**89**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 9:1) gave **88** as a colourless solid (236 mg, 62%, >98% de); mp 96 °C; $[\alpha]_D^{23}$ +133.5 (*c* 0.6, $CHCl_3$); ν_{max} (KBr) 1749 (C=O); δ_H (400 MHz, $CDCl_3$) 0.81 (3H, s, C(5)*Me*$_A$), 1.46 (3H, s, C(5)*Me*$_B$), 4.31 (1H, s, C(4)*H*), 4.55 (1H, d, *J* 11.7, OC*H*$_A$), 4.95 (1H, d, *J* 11.7, OC*H*$_B$), 5.61 (1H, s, C(3′)*H*), 7.01–7.53 (20H, m, C(1′)*H*, *Ar*, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.0, 28.7, 69.1, 71.2, 73.7, 81.3, 122.2, 122.6, 124.0, 124.1, 125.3, 127.9, 128.1, 128.4, 128.5, 128.6, 128.8, 130.6 (quartet), 132.2, 134.4, 134.7, 135.8, 137.1, 140.3, 156.7; *m*/*z* (ESI$^+$) 616 ([M+59]$^+$, 100%); HRMS (FI$^+$) found 580.2076, $C_{34}H_{30}F_3NNaO_3^+$ ([M+Na]$^+$) requires 580.2070.

*4.4.43.1. X-ray crystal structure determination for **88**.* Data were collected using an Enraf–Nonius κ-CCD diffractometer with graphite monochromated Mo Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[42]

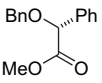
X-ray crystal structure data for **88** [$C_{34}H_{30}F_3NO_3$]: *M*=557.61, monoclinic, space group $P12_11$, *a*=11.59210(10) Å, *b*=12.77350(10) Å, *c*=19.7303(2) Å, β=98.0963(4)°, *V*=2892.38(4) Å^3, *Z*=4, μ=0.094 mm^{-1}, colourless plate, crystal dimensions=0.1×0.1×0.2 mm^3. A total of 6850 unique reflections were measured for $5<\theta<27$ and 5452 reflections were used in the refinement. The final parameters were wR_2=0.176 and R_1=0.118 [$I>0.5\sigma(I)$]. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 653143. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

*4.4.44. (4S,2′R)-N(3)-(2′-Benzyloxy-2′-phenyl-acetyl)-4-phenyl-5,5-dimethyl-oxazolidin-2-one **94***



$NaIO_4$ (120 mg, 0.56 mmol) was added to a vigorously stirred solution of **84** (100 mg, 0.20 mmol) in CCl_4 (2 mL), MeCN (2 mL) and H_2O (3 mL). $RuCl_3$ (2.2 mg, 0.01 mmol) was added and the solution stirred at rt for 12 h after which time H_2O (15 mL) was added and the mixture extracted with EtOAc (3×10 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 3:1) gave **94** as a colourless oil (76 mg, 92%); $[\alpha]_D^{23}$ −4.9 (*c* 1.3, $CHCl_3$); ν_{max} (film) 1775 (C=O), 1716 (C=O); δ_H (400 MHz, $CDCl_3$) 0.88 (3H, s, C(5)*Me*$_A$), 1.60 (3H, s, C(5)*Me*$_B$), 4.58 (2H, d, *J* 3.2, OC*H*$_2$), 5.14 (1H, s, C(4)*H*), 6.37 (1H, s, C(2′)*H*), 6.57–7.62 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.9, 29.1, 66.9, 71.4, 79.0, 82.9, 127.8, 128.2, 128.4, 128.5, 129.0, 130.2, 135.0, 135.1, 137.4, 152.5, 170.4; *m*/*z* (CI$^+$) 433 ([M+NH_4]$^+$, 100%); HRMS (CI$^+$) found 433.2123, $C_{26}H_{29}N_2O_4^+$ ([M+NH_4]$^+$) requires 433.2122.

*4.4.45. Methyl (R)-2-benzyloxy-2-phenylacetate **95***



A solution of **94** (70 mg, 0.17 mmol) in MeOH (1 mL) was added to a 0.1 M solution of MeOMgBr [3.1 mL, 0.34 mmol; prepared by addition of MeMgBr (0.1 mL, 0.84 mmol) to MeOH (3 mL)] at 0 °C. After stirring for 20 min, satd aq NH_4Cl (2 mL) was added and the mixture was extracted with Et_2O (3×5 mL). The combined organic extracts were dried and concentrated in vacuo. Purification via

flash column chromatography (eluent 30–40 °C petrol/Et_2O, 1:1) gave **95** as a colourless oil (34 mg, 79%); $[\alpha]_D^{23}$ −84.9 (*c* 1.15, $CHCl_3$) {lit.[40] for >99% ee $[\alpha]_D^{20}$ −95.9 (*c* 1.1, $CHCl_3$)}; δ_H (500 MHz, $CDCl_3$) 3.78 (3H, s, O*Me*), 4.66 (2H, ABq, OCH_2), 5.01 (1H, s, C(2)*H*), 7.31–7.67 (10H, m, *Ph*).

References and notes

1. Nelson, W. L.; Wennerstrom, J. E.; Sankar, S. R. *J. Org. Chem.* **1977**, *42*, 1006; Rao, A. V. R.; Bose, D. S.; Gurjar, M. K.; Ravindranathan, T. *Tetrahedron* **1989**, *45*, 7031; Wright, A. E.; Schafer, M.; Midland, S.; Munnecke, D. E.; Sims, J. J. *Tetrahedron Lett.* **1989**, *30*, 5699; Parida, S.; Dordick, J. S. *J. Am. Chem. Soc.* **1991**, *113*, 2253; Bianchi, D.; Bosetti, A.; Cesti, P.; Golini, P. *Tetrahedron Lett.* **1992**, *33*, 3231.
2. For instance, see: Lohray, B. B.; Ahuja, J. R. *J. Chem. Soc., Chem. Commun.* **1991**, 95; Kolb, H. C.; Sharpless, K. B. *Tetrahedron* **1992**, *48*, 10515; Nicolaou, K. C.; Huang, X.; Snyder, S. A.; Rao, P. B.; Bella, M.; Reddy, M. V. *Angew. Chem., Int. Ed.* **2002**, *41*, 834.
3. For syntheses of terminal 1,2-diols, see: Colombo, L.; Di Giacomo, M.; Brusotti, G.; Milano, E. *Tetrahedron Lett.* **1995**, *36*, 2863; Cho, B. T.; Chun, Y. S. *Tetrahedron: Asymmetry* **1999**, *10*, 1843; Smyj, R. P.; Chong, J. M. *Org. Lett.* **2001**, *3*, 2903; Gómez, A. M.; Company, M. D.; Valverde, S.; López, J. C. *Org. Lett.* **2002**, *4*, 383; Kamal, A.; Sandbhor, M.; Ahmed, K.; Adil, S. F.; Shaik, A. A. *Tetrahedron: Asymmetry* **2003**, *14*, 3861; Cho, B. T.; Choi, O. K.; Kim, D. J. *Bull. Korean Chem. Soc.* **2003**, *24*, 1023.
4. For a review on asymmetric dihydroxylation, see: Kolb, H. C.; Vannieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.
5. For epoxidations of chiral enamides, see: (a) Xiong, H.; Hsung, R. P.; Shen, L.; Hahn, J. M. *Tetrahedron Lett.* **2002**, *43*, 4449; (b) Adam, W.; Bosio, S. G.; Wolff, B. T. *Org. Lett.* **2003**, *5*, 819; (c) Adam, W.; Bosio, S. G.; Turro, N. J.; Wolff, B. T. *J. Org. Chem.* **2004**, *69*, 1704; (d) Sivaguru, J.; Saito, H.; Poon, T.; Omonuwa, T.; Franz, R.; Jockusch, S.; Hooper, C.; Inoue, Y.; Adam, W.; Turro, N. J. *Org. Lett.* **2005**, *7*, 2089; For α-metallation of chiral enamides, see: Lander, P. A.; Hegedus, L. S. *J. Am. Chem. Soc.* **1994**, *116*, 8126; For [2+2] cycloadditions of chiral enamides, see: Hegedus, L. S.; Bates, R. W.; Söderberg, B. C. *J. Am. Chem. Soc.* **1991**, *113*, 923; Hegedus, L. S. *Tetrahedron* **1997**, *53*, 4105; Riches, A. G.; Wernersbach, L. A.; Hegedus, L. S.; Bach, T.; Schroder, J.; Brandl, T.; Hecht, J.; Harms, K. *Tetrahedron* **1998**, *54*, 4507; Bach, T.; Schroder, J.; Brandl, T.; Hecht, J.; Harms, K. *Tetrahedron* **1998**, *54*, 4507; Adam, W.; Bosio, S. G.; Turro, N. J. *J. Am. Chem. Soc.* **2002**, *124*, 8814; For cyclopropanations of chiral enamides, see: Song, Z.; Lu, T.; Hsung, R. P.; Al-Rashid, Z. F.; Ko, C.; Tang, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 4069; Voigt, J.; Noltemeyer, M.; Reiser, O. *Synlett* **1997**, 202; Akiba, T.; Tamura, O.; Hashimoto, M.; Kobayashi, Y.; Katoh, T.; Nakatani, K.; Kamada, M.; Hayakawa, I.; Terashima, S. *Tetrahedron* **1994**, *50*, 3905; Seebach, D.; Stucky, G.; Pfammatter, E. *Chem. Ber.* **1989**, *122*, 2377; Seebach, D.; Stucky, G. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1351; For Diels–Alder cycloadditions with chiral enamides, see: Gohier, F.; Bouhadjera, K.; Faye, D.; Gaulon, C.; Maisonneuve, V.; Dujardin, G.; Dhal, R. *Org. Lett.* **2007**, *9*, 211; Crawly, S. L.; Funk, R. L. *Org. Lett.* **2006**, *8*, 3995; Palasz, A. *Org. Biomol. Chem.* **2005**, *3*, 3207; Robiette, R.; Cheboub-Benchaba, K.; Peeters, D.; Marchand-Brynaert, J. *J. Org. Chem.* **2003**, *68*, 9809; Huang, J.; Xiong, H.; Hsung, R. P.; Rameshkumar, C.; Mulder, J. A.; Grebe, T. P. *Org. Lett.* **2002**, *4*, 2417; Abbiati, G.; Clerici, F.; Gelmi, M. L.; Gambini, A.; Pilati, T. *J. Org. Chem* **2001**, *66*, 6299.
6. Adam, W.; Peters, E.-M.; Peters, K.; von Schnering, H. G.; Voerckel, V. *Chem. Ber.* **1992**, *125*, 1263; Adam, W.; Ahrweiler, M.; Paulini, K.; Reissig, H.-U.; Voerckel, V. *Chem. Ber.* **1992**, *125*, 2719.
7. Barton, D. H. R.; Motherwell, W. B.; Zard, S. Z. *J. Chem. Soc., Chem. Commun.* **1981**, 774; Zhang, X.; Foote, C. S. *J. Am. Chem. Soc.* **1993**, *115*, 8867; Adam, W.; Ahrweiler, M.; Sauter, M.; Schmiedeskamp, B. *Tetrahedron Lett.* **1993**, *34*, 5247; Adam, W.; Ahrweiler, M.; Peters, K.; Schmiedeskamp, B. *J. Org. Chem* **1994**, *59*, 2733; Adam, W.; Reinhardt, D. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1503.
8. Bach, J.; Bull, S. D.; Davies, S. G.; Nicholson, R. L.; Sanganee, H. J.; Smith, A. D. *Tetrahedron Lett.* **1999**, *40*, 6677.
9. For a related approach, see: Gaul, C.; Scharer, K.; Seebach, D. *J. Org. Chem* **2001**, *66*, 3059.
10. Davies, S. G.; Key, M.-S.; Rodriguez-Solla, H.; Sanganee, H. J.; Savory, E. D.; Smith, A. D. *Synlett* **2003**, 1659.
11. For a review of chiral auxiliary directed epoxidations, see: Adam, W.; Zhang, A. *Synlett* **2005**, 1047.
12. SuperQuat **13** was prepared from (*S*)-phenylglycine according to the procedure of Bull, S. D.; Davies, S. G.; Jones, S.; Polywka, M. E. C.; Prasad, R. S.; Sanganee, H. J. *Synlett* **1998**, 519.
13. Zezza, C. A.; Smith, M. B. *Synth. Commun.* **1987**, *17*, 729.
14. Jiang, L.; Job, G. E.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 3667.
15. DMDO was prepared and titrated according to the procedures outlined by Adam et al.; see: (a) Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377; (b) Adam, W.; Chan, Y.-Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800.
16. Epoxide **19** proved susceptible to hydrolysis upon standing.
17. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 213199, see Ref. 10.
18. For instance, regioselective S_N2 epoxide opening of epoxide (4*S*,1′*R*,2′*S*)-**19** at C(1′) would be expected to furnish (4*S*,1′*S*,2′*S*)-**22**; instead (4*S*,1′*R*,2′*S*)-**21** is observed as the major product.
19. Compound **31** was prepared from SuperQuat **13** according to the procedure of McAlonan, H.; Murphy, J. P.; Nieuwenhuyzen, M.; Reynolds, K.; Sarma, P. K. S.; Stevenson, P. J.; Thompson, N. *J. Chem. Soc., Perkin Trans. 1* **2002**, 69.
20. Wittig reactions employing **31** were found to be highly sensitive to the presence of water, with *N*-methyl SuperQuat (*N*(3)-methyl-4-phenyl-5,5-dimethyl-oxazolidin-2-one) being isolated as a side product on occasion.
21. Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.
22. For instance, see: Podraza, K. F.; Naworal, J. D. *J. Agric. Food Chem.* **1986**, *34*, 841; Matchett, S. A.; Norton, J. R.; Anderson, O. P. *Organometallics* **1988**, *7*, 2228.
23. For instance, see: Van der Louw, J.; Komen, C. M. D.; Knol, A.; De Kanter, F. J. J.; Van der Baan, J. L.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron Lett.* **1989**, *30*, 4453.
24. For instance, see: Colombo, L.; Di Giacomo, M. *Tetrahedron Lett.* **1999**, *40*, 1977; Choi, I.-Y.; Lee, H. G.; Chung, K.-H. *J. Org. Chem.* **2001**, *66*, 2484; Prasad, K. R.; Anbarasan, P. *Tetrahedron: Asymmetry* **2005**, *16*, 3951.
25. Riehl, J.; Fougerousse, A. *Bull. Soc. Chim. Fr.* **1968**, *10*, 4083.
26. Kim, J.-H.; Yang, H.; Park, J.; Boons, G.-J. *J. Am. Chem. Soc.* **2005**, *127*, 12090.
27. Golding, B. T.; Hall, D. R.; Sakrikar, S. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1214.
28. Bergstein, W.; Kleemann, A.; Martens, J. *Synthesis* **1981**, 76.
29. A similar observation has been reported by Hsung et al., see Ref. 5a.
30. Mursakulov, I. G.; Guseinov, M. M.; Kasumov, N. K.; Zefirov, N. S.; Samoshin, V. V.; Eliel, E. L. *Tetrahedron* **1980**, *36*, 1885; Mursakulov, I. G.; Guseinov, M. M.; Kasumov, N. K.; Zefirov, N. S.; Samoshin, V. V.; Chalenko, E. G. *Tetrahedron* **1982**, *38*, 2213.
31. Lee, L. G.; Whitesides, G. M. *J. Org. Chem.* **1986**, *51*, 25.
32. Hayashi, Y.; Yamaguchi, J.; Sumiya, T.; Hibino, K.; Shoji, M. *J. Org. Chem* **2004**, *69*, 5966.
33. In addition to epimerisation, **63** has been shown to be unstable to dimerisation, see: Boutoute, P.; Mousset, G.; Veschambre, H. *New J. Chem.* **1998**, *22*, 247.
34. Keiji, M.; Masataka, O.; Hisashi, Y. *Synlett* **1993**, 693.
35. See Ref. 9. Gawley, R. E.; Campagna, S. A.; Santiago, M.; Ren, T. *Tetrahedron: Asymmetry* **2002**, *13*, 29.
36. Enamide **72** was prepared according to the procedure of Brice, J. L.; Meerdink, J. E.; Stahl, S. S. *Org. Lett.* **2004**, *6*, 1845.
37. The γ-deprotonation of *N*-acyl enamides has been documented, see: Gaul, C.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 963.
38. Jatzke, H.; Evertz, U.; Scmidt, R. R. *Synlett* **1990**, 191.
39. Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.
40. Effenberger, F.; Hopf, M.; Ziegler, T.; Hudelmayer, J. *Chem. Ber.* **1991**, *124*, 1651.
41. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.
42. Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, C. K.; Watkin, D. J. *Crystals*; Department of Chemical Crystallography, Chemistry Research Laboratory, University of Oxford: UK, 2001.
43. Hashimoto, S.; Furukawa, I. *Phosphorus Sulfur* **1978**, *4*, 129.
44. Freire, F.; Seco, J. M.; Quiñoá, E.; Riguera, R. *Chem.—Eur. J.* **2005**, *11*, 5509.
45. For ^1H and ^{13}C NMR chemical shifts, see Ref. 28; Cardillo, G.; Orena, M.; Romero, M.; Sandri, S. *Tetrahedron* **1989**, *45*, 1501.
46. Guette, J. P.; Spassky, N. *Bull. Soc. Chim. Fr.* **1972**, 4217.