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Enantioselective N-heterocyclic carbene catalyzed formal [3+2] cycloaddition using α-aroyloxyaldehydes and oxaziridines

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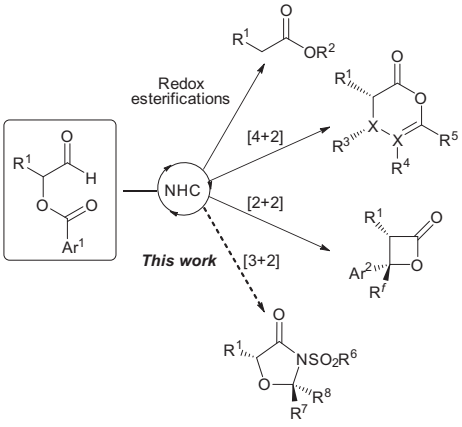
ABSTRACT

An enantioselective N-heterocyclic carbene catalysed formal [3+2] cycloaddition has been developed for the synthesis of oxazolindin-4-one products. The reaction of oxaziridines and α-aroyloxyaldehydes under N-heterocyclic carbene catalysis provides the formal cycloaddition products with excellent control of the diastereo- and enantioselectivity (12 examples, up to >95:5 dr, >99:1 er). A matched-mismatched effect between the enantiomer of the catalyst and oxaziridine was identified, and preliminary mechanistic studies have allowed the proposal of a model to explain these observations.

1. Introduction

N-Heterocyclic carbenes (NHCs) occupy a privileged position within the field of Lewis base organocatalysis due to the wide range of reactive intermediates accessible from readily available starting materials.[1] Beyond the classical acyl anion equivalent reactivity mode, the development of NHC catalysis has resulted in numerous methods that proceed by acyl azolium, α,β-unsaturated acyl azolium, azolium enolate, homoenolate and radical cation intermediates.[1,2] Within this field, azolium enolates have been applied to a range of reactions, including highly enantio- and diastereoselective intramolecular cyclizations,[3] desymmetrizations,[4] and (formal) [4+2],[5] [2+2],[6] and to a lesser extent [3+2] cycloadditions.[7] Traditionally, azolium enolate species have been generated from the direct addition of NHCs to ketenes,[6b,c] however the inherent difficulties associated with substrate synthesis and stability has resulted in the development of alternative methods.[2] The most common approach to azolium enolate intermediates is through the use of NHC redox catalysis, in which α-functionalized aldehydes (such as α-haloaldehydes, α-aryloxyaldehydes or epoxyaldehydes) or enals are used. In previous work we introduced the use of α-aroyloxyaldehydes in NHC redox catalysis.[8] These serve as bench-stable alternatives to α-haloaldehydes that are traditionally difficult to prepare and store. To date, α-aroyloxyaldehydes have been applied for the NHC-catalyzed synthesis of esters and amides,[8] including application in the acylative kinetic resolutions of alcohols,[9] and as azolium enolate precursors in enantio- and diastereoselective [4+2] and [2+2] cycloadditions (Scheme 1).[8,10]



Scheme 1. Applications of α-aroyloxyaldehydes in NHC redox catalysis.

The development of stereoselective methods for the synthesis of heterocyclic compounds is a major area of chemical research due to their ubiquitous use in pharmaceuticals and agrochemicals. Natural products containing the oxazolidin-4-one core structure have only recently been isolated, and show promising levels of anti-bacterial and anti-fungal activity.[11] The development of new

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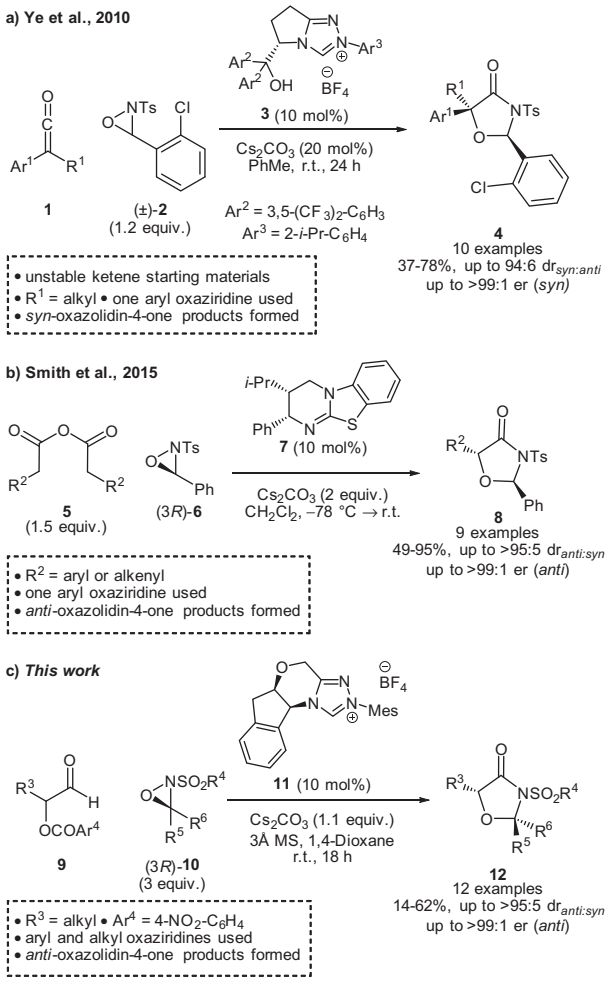
catalytic stereoselective methods for the synthesis of oxazolidin-4-ones is therefore of interest to allow broader access to these bioactive heterocyclic compounds. Recently, a number of methods for the stereoselective synthesis of oxazolidin-4-ones have been reported involving oxidation of a catalytically-generated enolate with an oxaziridine in a formal [3+2] cycloaddition (Scheme 2).[12] In 2010, Ye et al. reported the formal [3+2] cycloaddition between ketenes **1** and oxaziridines **2** using either an NHC or cinchona alkaloid catalyst (Scheme 2, a).[13] α,α-Disubstituted *syn*-oxazolidin-4-one products **4** were obtained in good yield and with generally high diastereo- and enantiocontrol using racemic 2-chlorophenyl oxaziridine derivative (±)-**2**. Notably, when using 1.2 equivalents of the oxaziridine (±)-**2**, enantioenriched oxaziridine was recovered from the reaction, which is indicative of a kinetic resolution process.[14] The scope of this method is limited however by the stability and range of ketene precursors available. We have recently reported a complementary isothiourea-catalyzed method using homoanhydrides **5** as the ammonium enolate precursor to give *anti*-oxazolidin-4-one products **8** (Scheme 2, b).[15] In this method, the use of racemic oxaziridine led to products with high enantioselectivity, but low diastereoselectivity. The use of enantiopure oxaziridine gave *anti*-oxazolidin-4-ones **8** with high enantio- and diastereoselectivity, consistent with conservation of the oxaziridine stereocentre throughout the reaction process. Although a number of examples were reported, this method was limited to aryl- and vinylacetic acid-derived homoanhydrides **5**, and again the use of only a single oxaziridine **6** was demonstrated. Feng and Liu have developed an alternative method using Brønsted base-catalyzed oxyamination of azalactones using a range of oxaziridines.[16] By using 2 equivalents of racemic oxaziridine an efficient kinetic resolution of the oxaziridine was also realized, with selectivity factors of up to 52 being reported.[14]

Building upon these precedents, herein the expansion of the range of methods available for the generation of enantioenriched oxazolidin-4-one products is investigated through the use of α-aroyloxyaldehydes as bench-stable azolium enolate precursors in NHC redox catalysis (Scheme 2, c). This approach allows access to *anti*-5-alkyl-oxazolidin-4-one products, previously inaccessible in enantioenriched form using organocatalytic methods.

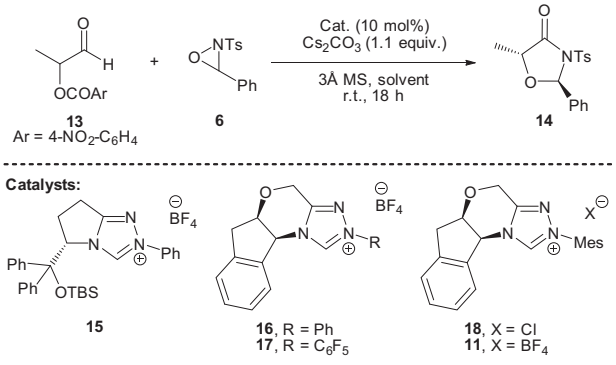


Scheme 2. Lewis-base catalyzed methods for the stereoselective synthesis of oxazolidin-4-one derivatives.

2. Results and discussion

Initial studies focused on the optimization of the reaction of α-aroyloxyaldehyde **13** with racemic oxaziridine (±)-**6** using different N-heterocyclic carbene precursors. Using L-pyroglutamic acid derived triazolium **15**, which had shown activity in Ye's formal [3+2] cycloaddition methodology using ketenes,[13] gave no product (Table 1, entry 1). Aminoindanol-derived catalysts **16**–**18** were next studied due to previous activity in catalyzing formal [4+2] and [2+2] cycloadditions using α-aroyloxyaldehydes (entries 2–4).[10] Of these, *N*-mesityl-substituted triazolium **18** gave *anti*-oxazolidin-4-one **14** in the highest yield (entry 4). Using enantioenriched oxaziridine (3*R*)-**6** and exchanging the counterion of the triazolium salt from chloride **18** to tetrafluoroborate **11** resulted in an increase in diastereoselectivity, giving oxazolidin-4-one **14** as essentially a single diastereo- and enantiomer (entries 5–6).

Table 1
Reaction optimization[a]



Entry	Cat.	**13** (equiv)	**6** (equiv)	Solvent	Yield[b] (%)	dr[c]	er[d]
1	**15**	1.5	1 (±)	THF	0	–	–
2	**16**	1.5	1 (±)	THF	8 (25)	63:37	ND[e]
3	**17**	1.5	1 (±)	THF	2 (19)	83:17	ND[e]
4	**18**	1.5	1 (±)	THF	27 (49)	81:19	ND[e]
5	**18**	1.5	1 (3*R*)	THF	21 (47)	93:7	98:2
6	**11**	1.5	1 (3*R*)	THF	23 (51)	>95:5	99:1
7	**11**	1	2 (3*R*)	THF	23 (53)	>95:5	>99:1
8	**11**	1	2 (3*R*)	1,4-Dioxane	36 (62)	>95:5	>99:1
9	**11**	1	3 (3*R*)	1,4-Dioxane	44 (78)	>95:5	>99:1
10	**11**	1	3 (±)	1,4-Dioxane	30	78:22	95:5

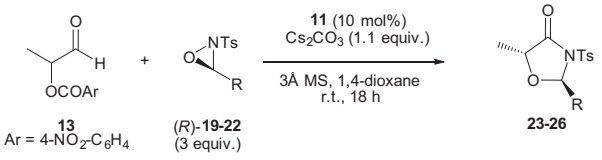
[a] Reactions were performed on a 0.2 mmol scale, in flame-dried glassware and under an argon atmosphere.
[b] Isolated yield. Yields determined by quantitative ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard given in parentheses.
[c] Determined by ^{1}H NMR spectroscopy of the crude reaction mixture.
[d] Determined by chiral HPLC analysis of the isolated product.
[e] ND = not determined.

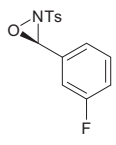
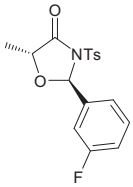
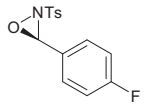
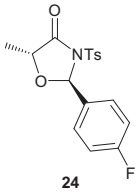
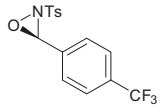
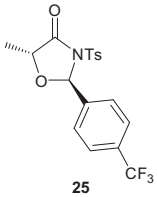
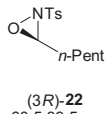
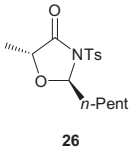
The absolute configuration of the product was confirmed by single crystal X-ray analysis.[17] Finally, increasing the equivalents of oxaziridine (3*R*)-**6** and by using 1,4-dioxane as the solvent gave oxazolidin-4-one **14** in an improved isolated yield (44%, entries 7–9). Analytically pure product was obtained using a sodium bisulfite wash to remove imine and aldehyde side-products, followed by flash silica column chromatography. Analysis of the crude reaction mixture by quantitative ^{1}H NMR spectroscopy however identified a much higher yield (78%), indicating that the moderate isolated yields were a result of difficulties in product isolation. The use of racemic oxaziridine (±)-**6** under the optimized reaction conditions gave oxazolidin-4-one **14** with lower diastereo- and enantiocontrol (entry 10). This demonstrates the importance of using enantioenriched oxaziridine in this process, and indicates a more productive and selective reaction takes place between the azolium enolate derived from the (5a*R*,10b*S*)-enantiomer of the N-heterocyclic carbene and the (*R*)-enantiomer of the oxaziridine. However, in these reactions the oxaziridine was fully consumed (to give the corresponding imine), and thus the potential for a kinetic resolution process could not be assessed.

As previous methods focused on the use of a single aryl-substituted oxaziridine, the use of alternative oxaziridines was investigated. Based on the optimization studies it was reasoned that enantioenriched oxaziridines were needed for this study. Using a modification of Jørgensen's cinchona alkaloid-catalyzed oxaziridination of imines,[18] in which hydroquinidine was used in place of the optimal catalyst, a selection of enantioenriched oxaziridines were synthesized and tested in the developed methodology (Table 2). Enantioenriched 3- and 4-fluorophenyl-substituted oxaziridines **19** and **20** (88:12 and 87:13 er, respectively) gave oxazolidin-4-ones **23** and **24** in moderate yield but with excellent diastereo- and enantiocontrol (entries 1–2). 4-Trifluorophenyl-substituted oxaziridine **21** could only be isolated in 78.5:21.5 er, and accordingly oxazolidin-4-one product **25** was obtained with slightly lower diastereoselectivity, but still with excellent enantioselectivity (entry 3). The use of an alkyl-substituted oxaziridine **22** was also investigated. Although oxaziridine **22** was only obtained in 60.5:39.5 er, the oxazolidin-4-one product **26** was still generated in good yield and with good diastereoselectivity and excellent enantioselectivity (entry 4). Alternative enantioenriched oxaziridines, including those bearing electron-donating groups, could not be synthesized in sufficiently enantioenriched form to be synthetically useful in this methodology.[19]

The application of a variety of α-aroyloxyaldehydes in the developed method was next investigated using oxaziridine (3*R*)-**6** to give a range of 5-alkyl-substituted oxazolidin-4-one products (Table 3). 5-Benzyl-substituted oxazolidin-4-ones **33**–**35** bearing ether and acetal functional groups were obtained in moderate yields but with excellent diastereo- and enantiocontrol. Extended alkyl chains were also introduced, including those bearing protected alcohol and amine functionalities, to give oxazolidin-4-ones **36**–**38** with similarly high levels of diastereo- and enantiocontrol.

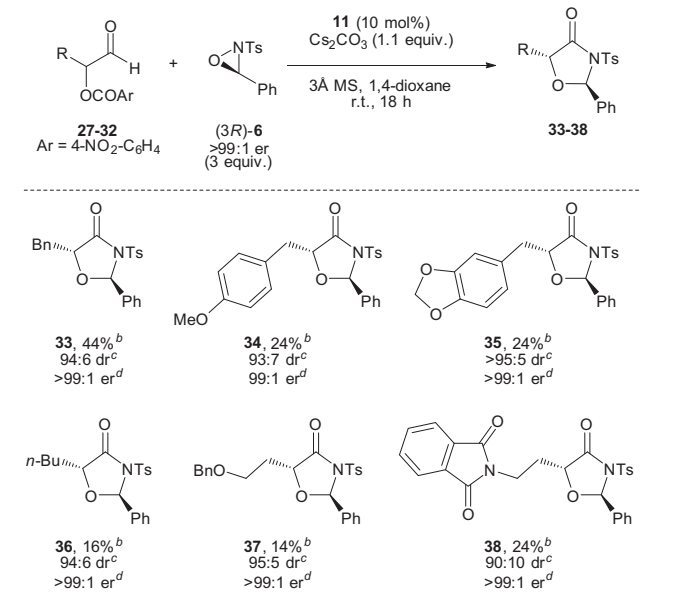
Table 2
Reaction scope: variation of oxaziridine[a]



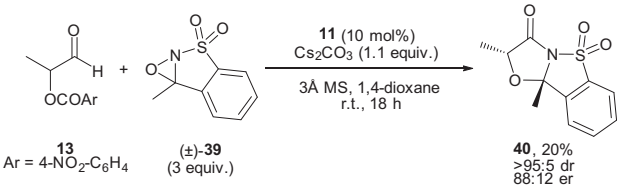
Entry	Oxaziridine	Product	Yield[b] (%)	dr[c]	er[d]
1	 (3*R*)-**19** 88:12 er	 **23**	46	93:7	98.5:1.5
2	 (3*R*)-**20** 87:13 er	 **24**	28	>95:5	>99:1
3	 (3*R*)-**21** 78.5:21.5 er	 **25**	40	90:10	97.5:2.5
4	 (3*R*)-**22** 60.5:39.5 er	 **26**	62	80:20	94:6

[a] Reactions conditions: **13** (0.2 mmol), oxaziridine (3*R*)-**19**–**22** (0.6 mmol), **11** (0.02 mmol), Cs_2CO_3 (0.22 mmol), 1,4-dioxane (0.05 M), rt, 18 h.
[b] Isolated yield.
[c] Determined by ^{1}H NMR spectroscopy of the crude reaction mixture.
[d] Determined by chiral HPLC analysis of the isolated product.

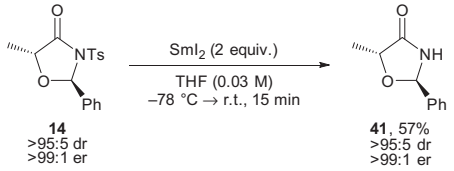
Table 3
Reaction scope: variation of α-aroyloxyaldehyde[a]



[a] Reactions conditions: **27**–**32** (0.2 mmol), oxaziridine (3*R*)-**6** (0.6 mmol), **11** (0.02 mmol), Cs_2CO_3 (0.22 mmol), 1,4-dioxane (0.05 M), rt, 18 h.
[b] Isolated yield.
[c] Determined by ^{1}H NMR spectroscopy of the crude reaction mixture.
[d] Determined by chiral HPLC analysis of the isolated product.



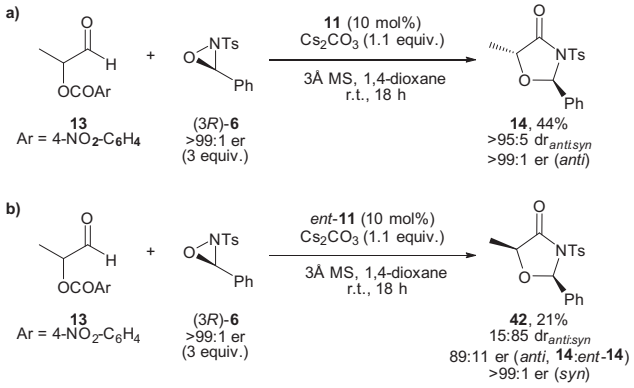
Scheme 3. NHC-catalyzed formal [3+2] cycloaddition using ketimine-derived oxaziridine (±)-**39**.



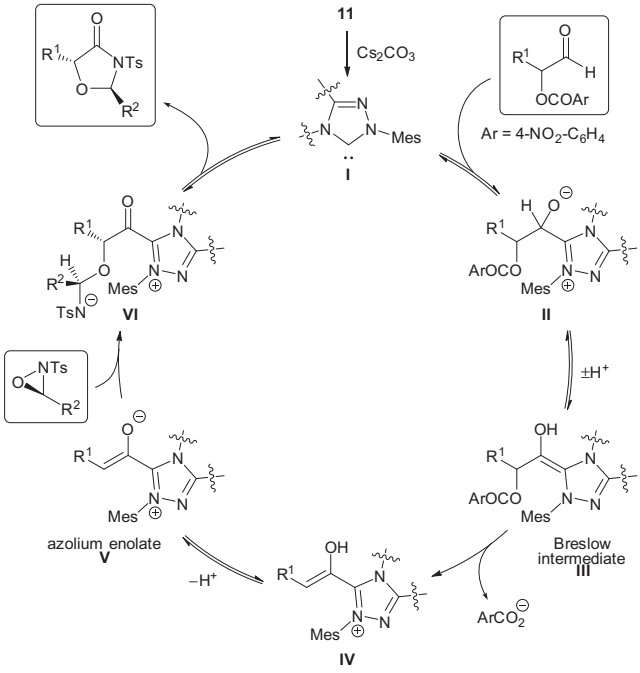
Scheme 4. *N*-Detosylation of oxazolidin-4-one **14** using samarium(II) iodide.

To extend the scope of the developed method beyond those previously reported, the use of ketimine-derived oxaziridines was investigated. Under the standard reaction conditions, the use of oxaziridine (±)-**39** synthesized from saccharin in two steps gave 2,2-disubstituted oxazolidin-4-one **40** in moderate yield but with good enantio- and excellent diastereoselectivity (Scheme 3). The relative configuration of the product was assigned using nOe spectroscopy,[20] and the absolute configuration assigned by analogy to oxazolidin-4-one **14**. The 2,2-disubstituted oxazolidin-4-one **40** was only metastable and so the configuration could not be further confirmed using single crystal X-ray analysis. The removal of the *N*-tosyl group of the oxazolidinone products was also demonstrated using samarium(II) iodide (Scheme 4). The deprotected oxazolidin-4-one **41** was obtained in good yield and with complete retention of diastereo- and enantiopurity.

Finally, we sought to provide some insight into the mechanism of the reaction (Scheme 5). During optimization studies, the use of enantioenriched oxaziridine (3*R*)-**6** was essential for high diastereo- and enantioselectivity (Table 1, entries 9–10, Scheme 5, a). The apparent synergistic effect between the configuration of the catalyst and oxaziridine was further probed by performing the reaction using the opposite enantiomer of the catalyst *ent*-**11** with enantioenriched oxaziridine (3*R*)-**6** (Scheme 5, b). The *syn*-oxazolidin-4-one product **42** was obtained (15:85 $dr_{anti:syn}$) in lower yield but with excellent enantioselectivity (>99:1 er). The absolute configuration of the major product obtained using either enantiomer of the NHC pre-catalyst, **11** or *ent*-**11**, and oxaziridine (3*R*)-**6** (Scheme 5, a and b) can be explained by the catalyst controlling the configuration of the C(5) position, whilst the configuration of the C(2) position is defined by the configuration of the oxaziridine. The lower yield and diastereoselectivity obtained using (*ent*)-**11** and oxaziridine (3*R*)-**6** is indicative of a mismatched effect. The absolute configuration of the minor *anti*-product **14** obtained was the same as that obtained using pre-catalyst **11**, thus indicating that in the mismatched case, the stereocentre present in the oxaziridine overrides the usual facial selectivity observed using azolium enolates derived from the (5a*S*,10b*R*)-enantiomer of the NHC. These results are consistent with the configuration of the oxaziridine stereocentre being conserved. This contrasts the mechanism proposed by Ye et al. for the formal [3+2] cycloaddition between ketenes and oxaziridines using an NHC catalyst, in which α-oxidation of the azolium enolate to provide an oxirane and achiral imine was proposed, followed by recombination of the two



Scheme 5. Investigation of matched/mismatched effects, using (a) pre-catalyst **11** and oxaziridine (3*R*)-**6** (matched); and (b) pre-catalyst *ent*-**11** and oxaziridine (3*R*)-**6** (mismatched).



Scheme 6. Proposed mechanism.

intermediates to give the final oxazolidin-4-one product.[13] Although we cannot rule out a similar mechanism herein, the retention of configuration from the C(3) position of the oxaziridine to the C(2) position of the oxazolidin-4-one is most easily explained by direct chirality transfer in which the configuration of the stereocentre is conserved throughout the process.

Based on these observations, a mechanism for the formal [3+2] cycloaddition may be proposed (Scheme 6). Deprotonation of the triazolium salt **11** provides the free carbene **I**, which adds to the α-aroyloxyaldehyde to give adduct **II**. Proton transfer gives Breslow intermediate **III**, which followed by elimination of *para*-nitrobenzoate gives azolium enol **IV**. Deprotonation provides the key azolium enolate **V**. Nucleophilic attack on the oxaziridine at the oxygen results in α-oxidation of the azolium enolate and N—O bond cleavage of the oxaziridine to give zwitterionic acyl azolium intermediate **VI**. Finally, lactamization provides the oxazolidin-4-one product and regenerates the free carbene **I**.

3. Conclusion

An asymmetric N-heterocyclic carbene catalyzed formal [3+2] cycloaddition has been developed using α-aroyloxyaldehydes and oxaziridines. A range of oxazolidin-4-one products, previously inaccessible in enantioenriched form using organocatalysis, were obtained with excellent control of diastereo- and enantioselectivity. The use of a ketimine-derived oxaziridine was also demonstrated, providing access to enantiomerically-enriched 2,2-disubstituted oxazolidin-4-one products. *N*-Detosylation of the oxazolidin-4-one products was shown to proceed with retention of stereochemical purity, and preliminary mechanistic studies have allowed the proposal of a catalytic cycle.

4. Experimental

4.1. General

Reactions involving moisture sensitive reagents were carried out under an argon atmosphere using standard vacuum line techniques. All glassware was flame-dried and cooled under vacuum. Solvents (tetrahydrofuran and toluene) were obtained anhydrous and purified by passage through an alumina column (Mbraun SPS-800). Anhydrous 1,4-dioxane was obtained by distillation over calcium hydride. All other solvents and commercial reagents were used as supplied without further purification. Room temperature (rt) refers to 20–25 °C. Temperatures of −40 °C were obtained using an immersion cooler and an acetone bath. Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 F254 silica). TLC visualization was carried out with ultraviolet light (254 nm), followed by staining with a 1% aqueous $KMnO_4$ solution. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated or on the Biotage® Isolera™ 4. ^1H, ^{13}C and ^{19}F nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker Avance II 400 (400 MHz, ^1H; 101 MHz, ^{13}C; 376 MHz, ^{19}F), Bruker Avance 500 (500 MHz, ^1H; 126 MHz, ^{13}C) or a Bruker Avance III 500 (500 MHz, ^1H; 126 MHz, ^{13}C) spectrometer at ambient temperature in the deuterated solvent stated. All chemical shifts are quoted in parts per million (ppm) relative to the residual solvent as the internal standard. All coupling constants, *J*, are quoted in Hz and determined by analysis using MestReNova v9.0.1 software. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets), dt (doublet of triplets), td (triplet of doublets), ddt (doublet of doublets of triplets), tdd (triplet of doublets of doublets) and qd (quartet of doublets). The abbreviation Ar is used to denote aromatic, br to denote broad and app. to denote apparent. Infrared spectra (ν_{max}) were recorded on a Shimadzu IRAffinity-1 Fourier transform infrared spectrophotometer using either thin films or solids with a Pike MIRacle™ ATR accessory. Analysis was performed with Shimadzu IRsolution v1.50 software and only the characteristic peaks are quoted. Melting points were recorded on an Electrothermal 9100 melting point apparatus and are uncorrected. HPLC analyses were obtained on a Shimadzu HPLC consisting of a Shimadzu DGU-20A5 degasser, Shimadzu LC-20AT liquid chromatograph, Shimadzu SIL-20AT auto sampler, Shimadzu CBM-20A communications bus module, Shimadzu SPD-M20A diode array detector, Shimadzu CTO-20A. Mass spectrometry (*m*/*z*) data were acquired either by: electrospray ionization (ESI) at the University of St Andrews using a Micromass LCT spectrometer; nanospray ionization (NSI) at the EPSRC National Mass Spectrometry Facility, Swansea, on a Thermofisher LTQ Orbitrap XL spectrometer; or atmospheric pressure chemical ionization (APCI) at the EPSRC National Mass Spectrometry Facility, Swansea, on a Waters Xevo G2-S spectrometer. Synthesis of aromatic imines,[21] aliphatic imines,[22] authentic racemic oxaziridines,[23] α-aroyloxyaldehydes[10a,10d] and N-heterocyclic carbene precatalysts (**15**,[24] **16**,[25] **17**[25] and **18**[26]) were synthesized using literature procedures.

4.2. Cl^- to BF_4^- anion exchange of N-heterocyclic carbine precatalyst 18 to 11

4.2.1. (5a*R*,10b*S*)-2-Mesityl-5a,10b-dihydro-4*H*,6*H*-indeno[2,1-*b*][1,2,4]triazolo[4,3-*d*][1,4]oxazin-2-ium tetrafluoroborate 11

(5a*R*,10b*S*)-2-Mesityl-5a,10b-dihydro-4*H*,6*H*-indeno[2,1-*b*][1,2,4]triazolo[4,3-*d*][1,4]oxazin-2-ium chloride **18** (467 mg, 1.27 mmol) was added to a suspension of sodium tetrafluoroborate (346 mg, 3.17 mmol) in acetone (10 mL) and heated at 50 °C for 18 h. The flask was cooled to rt and the suspension was filtered and washed with acetone (3 × 10 mL). The solvent was concentrated under vacuum to give a brown solid, which was dissolved in CH_2Cl_2 (10 mL) and filtered through Celite®. The Celite® was washed with CH_2Cl_2 (3 × 10 mL) and the solvent concentrated under vacuum to give title compound **11** as a colourless solid with spectroscopic data in accordance with the literature[9b] (499 mg, 1.19 mmol, 94%); $[\alpha]_D^{20}$ = +29.8 (*c* 0.50, $CHCl_3$); mp 262–263 °C {Lit.[9b] 270 °C}; ^1H NMR (400 MHz, d_6-DMSO) δ_H: 2.11 (6H, s, N(2)Ar(2,6)CH_3), 2.37 (3H, s, N(2)Ar(4)CH_3), 3.16 (1H, d, *J* 17.0, C(6)H^aH^b), 3.49 (1H, dd, *J* 17.0, 5.0, C(6)H^aH^b), 4.98 (1H, app. t, *J* 4.5, C(5a)*H*), 5.07 (1H, d, *J* 16.1, OC(4)H^aH^b), 5.26 (1H, d, *J* 16.1, OC(4)H^aH^b), 6.08 (1H, d, *J* 4.2, C(10b)*H*), 7.21 (2H, s, N(2)Ar(3,5)*H*), 7.31–7.49 (3H, m, Ar*H*), 7.60 (1H, d, *J* 7.5, Ar*H*), 11.12 (1H, s, C(1)*H*). ^{19}F NMR (376 MHz, d_6-DMSO) δ_F: −148.20, −148.25.

4.3. General procedure for the enantioenriched oxaziridine synthesis

The following is a modification of a procedure reported by Jørgensen et al.[18] Imine (1 equiv) was dissolved in toluene (0.1 M) and cooled at −40 °C using a cryogenic bath. Next *m*CPBA (⩽77%, ≈1.1 equiv.) and hydroquinidine (10 mol %) were added and the suspension was vigorously stirred for 24 h. The reaction mixture was warmed to rt and concentrated under vacuum. The crude residue was purified by flash chromatography to give the title compound.

4.3.1. (3*R*)-3-Phenyl-2-tosyl-1,2-oxaziridine (3*R*)-6

Using general procedure 4.3—(*E*)-*N*-benzylidene-4-toluenesulfonamide (3.7 g, 14.3 mmol), *m*CPBA (⩽77%, 5 g, 16.0 mmol), hydroquinidine (450 mg, 1.4 mmol) in toluene (140 mL) gave, after column chromatography (10% EtOAc in hexane) and recrystallization (EtOAc and hexane), the title compound (3*R*)-**6** as a colourless solid with spectroscopic data in accordance with the literature[15] (1.69 g, 6.15 mmol, 43%); $[\alpha]_D^{20}$ = +81.3° (*c* 1.00, $CHCl_3$); mp 82–84 °C {Lit.[15] 86–89 °C}; Chiral HPLC analysis Chiralpak AS-H (95:5 hexane:*i*-PrOH, flow rate 1.0 mL min^{-1}, 220 nm, 30 °C) t_R(*R*): 9.6 min, t_R(*S*): 14.0 min, >99:1 er; ^1H NMR (400 MHz, $CDCl_3$) δ_H: 2.50 (3H, s, ArCH_3). 5.46 (1H, s, C(3)C*H*), 7.55–7.36 (7H, m, Ar*H*), 7.90–7.96 (2H, m, SO_2Ar(2,6)*H*).

4.3.2. (3*R*)-2-Tosyl-3-(3-(fluoro)phenyl)-1,2-oxaziridine (3*R*)-19

Using general procedure 4.3—(*E*)-*N*-(3-fluorobenzylidene)-4-methylbenzenesulfonamide (2.09 g, 7.14 mmol), *m*CPBA (⩽77%, 2.40 g, 8 mmol), hydroquinidine (228 mg, 0.7 mmol) in toluene (70 mL) gave, after column chromatography (10% EtOAc in hexane) and recrystallization ($CHCl_3$ and hexane), the title compound (3*R*)-**19** as a colourless solid with spectroscopic data in accordance with the literature[16] (357 mg, 1.22 mmol, 17%); $[\alpha]_D^{20}$ = +70.5 (*c* 1.00, $CHCl_3$); mp 55–57 °C {Lit. mp unreported}; Chiral HPLC analysis

Chiralpak AD-H (95:5 hexane:*i*-PrOH, flow rate 1 mL min^{-1}, 211 nm, 40 °C) t_R(*S*): 7.9 min, t_R(*R*): 8.7 min, 88:12 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.50 (3H, s, ArCH_3), 5.45 (1H, s, C(3)*H*), 7.08–7.20 (2H, m, C(3)Ar(2,4)*H*), 7.28 (1H, app dt, *J* 7.7, 1.3, C(3)Ar(6)*H*), 7.39 (1H, app td, *J* 8.0, 5.5, C(3)Ar(5)*H*), 7.43–7.46 (2H, m, SO_2Ar(3,5)*H*), 7.90–7.95 (2H, m, SO_2Ar(2,6)*H*); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F: −111.6.

4.3.3. (3*R*)-2-Tosyl-3-(4-(fluoro)phenyl)-1,2-oxaziridine (3*R*)-20

Using general procedure 4.3—(*E*)-*N*-(4-fluorobenzylidene)-4-methylbenzenesulfonamide (4.18 g, 14.3 mmol), *m*CPBA (⩽77%, 4.8 g, 16 mmol), hydroquinidine (456 mg, 1.4 mmol) in toluene (140 mL) gave, after column chromatography (10% EtOAc in hexane) and recrystallization ($CHCl_3$ and hexane), the title compound (3*R*)-**20** as a colourless solid with spectroscopic data in accordance with the literature[27] (1.40 g, 4.77 mmol, 33%); $[\alpha]_D^{20}$ = +67.3 (*c* 1.00, $CHCl_3$); mp 80–82 °C {Lit. mp unreported}; Chiral HPLC analysis Chiralpak AS-H (95:5 hexane:*i*-PrOH, flow rate 1 mL min^{-1}, 201 nm, 40 °C) t_R(*S*): 6.2 min, t_R(*R*): 9.9 min, 87:13 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.50 (3H, s, ArCH_3), 5.44 (1H, s, C(3)C*H*), 7.02–7.10 (2H, m, C(3)Ar(3,5)*H*), 7.40–7.46 (4H, m, C(3)Ar(2,6)*H* +SO_2Ar(3,5)*H*), 7.90–7.95 (2H, m, SO_2Ar(2,6)*H*); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F: −108.2.

4.3.4. (3*R*)-2-Tosyl-3-(4-(trifluoromethyl)phenyl)-1,2-oxaziridine (3*R*)-21

Using general procedure 4.3—(*E*)-4-methyl-*N*-(4-(trifluoromethyl)benzylidene)benzenesulfonamide (1.63 g, 5 mmol), *m*CPBA (⩽77%, 1.5 g, 6 mmol), hydroquinidine (163 mg, 0.7 mmol) in toluene (50 mL) gave, after column chromatography (10% EtOAc in hexane) and recrystallization (EtOAc and hexane), the title compound (3*R*)-**21** as a colourless solid with spectroscopic data in accordance with the literature[28] (515 mg, 1.5 mmol, 30%); $[\alpha]_D^{20}$ = +7.8 (*c* 1.00, $CHCl_3$); mp 82–84 °C {Lit.[28] 87–90 °C}; Chiral HPLC analysis Chiralpak AS-H (95:5 hexane:*i*-PrOH, flow rate 1.0 mL min^{-1}, 201 nm, 40 °C) t_R(*R*): 7.5 min, t_R(*S*): 9.7 min, 78.5:21.5 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.51 (3H, s ArCH_3), 5.51 (1H, s, C(3)C*H*), 7.42–7.47 (2H, m, SO_2Ar(3,5)*H*), 7.55–7.60 (2H, m, C(3)Ar(2,6)*H*), 7.62–7.72 (2H, m, C(3)Ar(3,5)*H*), 7.90–7.95 (2H, m, SO_2Ar(2,6)*H*); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F: −63.0.

4.3.5. (3*R*)-3-Pentyl-2-tosyl-1,2-oxaziridine (3*R*)-22

Using general procedure 4.3—(*E*)-*N*-hexylidene-4-methylbenzenesulfonamide (3.61 g, 14.3 mmol), *m*CPBA (⩽77%, 4.8 g, 16 mmol), hydroquinidine (456 mg, 1.4 mmol) in toluene (140 mL) gave, after column chromatography (5% EtOAc in hexane), the title compound (3*R*)-**22** as a colourless oil (850 mg, 3.14 mmol, 22%); $[\alpha]_D^{20}$ = +21.5° (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralpak OJ-H (99:1 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 211 nm, 40 °C) t_R(*S*): 9.8 min, t_R(*R*): 11.2 min, 60.5:39.5 er; ν_{max} (thin film) 2957 (C—H), 2930 (C—H), 2860 (C—H), 1346 (C—N), 1165 (Ar—SO_2N), 1090 (C—O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 0.88 (3H, m, CH_2CH_3), 1.22–1.36 (2H, m, CH_2), 1.41–1.53 (4H, m, 2 × CH_2), 1.73–1.88 (2H, m, CH_2), 2.47 (3H, s, ArCH_3), 4.65 (1H, t, *J* 4.9, CH_2CHNO), 7.34–7.51 (2H, m, Ar(3,5)*H*), 7.70–8.06 (2H, m, Ar(2,6)*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 13.9 (CH_2CH_3), 21.8 (ArCH_3), 22.4 (CH_2), 23.3 (CH_2), 30.4 (CH_2), 31.3 (CH_2), 78.4 (*C*(3)H), 129.3 (Ar*C*(2,6)H), 130.0 (Ar*C*(3,5)H), 131.7 (Ar*C*(1)), 146.2 (Ar*C*(4)); HRMS (ESI$^+$) $C_{13}H_{19}NO_3SNa^+$ [M+Na]$^+$ requires 292.0978, found 292.0974 (−1.3 ppm).

4.4. General procedure for the synthesis of oxazolidin-4-one

To a flame-dried round bottom flask containing a stirrer bar and 3 Å molecular sieves were added α-aroyloxyaldehyde (0.2 mmol), oxaziridine (0.6 mmol), N-heterocyclic carbene precatalyst (10 mol%), cesium carbonate (0.22 mmol) and anhydrous 1,4-dioxane (4 mL) under an argon atmosphere. The reaction mixture was allowed to stir at rt for 18 h. Sodium bisulfite solution (4 mL, aq. 10% w/v) was added and the reaction stirred at rt for 4 h. The reaction mixture was diluted with Et_2O (10 mL) and washed sequentially with water (10 mL), saturated aqueous NH_4Cl (10 mL), saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography to give the title compound.

4.4.1. (2*R*,5*R*)-5-Methyl-2-phenyl-3-tosyloxazolidin-4-one 14

Using general procedure 4.4—(3*R*)-3-phenyl-2-tosyl-1,2-oxaziridine (3*R*)-**6** (165 mg, 0.6 mmol), 1-oxopropan-2-yl 4-nitrobenzoate **13** (45 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane: EtOAc (100:0 2 CV, 100:0 to 90:10 10 CV, 90:10 3 CV)], the title compound **14** (23 mg, 0.088 mmol, 44%) as an off-white crystalline solid. mp 112–115 °C; $[\alpha]_D^{20}$ = +45.2 (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (95:5 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 211 nm, 40 °C) t_R(2*R*,5*R*): 11.1 min, t_R(2*S*,5*S*): 21.7 min, >99:1 er; ν_{max} (thin film, $CHCl_3$) 1739 (C═O), 1371 (C—N), 1168 (Ar—SO_2N); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 1.42 (3H, d, *J* 6.8, C(5)CH_3), 2.41 (3H, s, ArCH_3), 4.53 (1H, qd, *J* 6.8, 1.1, C(5)*H*), 6.56 (1H, d, *J* 1.1, C(2)*H*), 7.13–7.24 (2H, m, N(3)SO_2Ar(3,5)*H*), 7.38–7.41 (4H, m, C(2)Ar(2,3,5,6)*H*), 7.47–7.42 (1H, m, C(2)Ar(4)*H*), 7.52–7.61 (2H, m, N(3)SO_2Ar(2,6)*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 17.0 (C(5)CH_3), 21.9 (ArCH_3), 73.6 (*C*(5)H), 90.7 (*C*(2)H), 127.2 (C(2)Ar*C*(2,6)H), 128.4 (N(3)SO_2Ar*C*(2,6)H), 128.8 (C(2)Ar*C*(3,5)H), 129.6 (N(3)SO_2Ar*C*(3,5)H), 130.1 (C(2)Ar*C*(4)H), 135.0 (N(3)SO_2-Ar*C*(1)), 136.8 (C(2)Ar*C*(1)), 145.7 (N(3)SO_2Ar*C*(4)), 171.1 (*C*(4)═O); HRMS (NSI$^+$) $C_{17}H_{18}NO_4S^+$ [M+H]$^+$ requires 332.0951, found 332.0952 (+0.3 ppm).

4.4.2. (2*R*,5*S*)-5-Methyl-2-phenyl-3-tosyloxazolidin-4-one 42

Using general procedure 4.4—(3*R*)-3-phenyl-2-tosyl-1,2-oxaziridine (3*R*)-**6** (165 mg, 0.6 mmol), 1-oxopropan-2-yl 4-nitrobenzoate **13** (45 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst *ent*-**11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 2 CV, 100:0 to 90:10 10 CV, 90:10 3 CV)], the title compound **42** as a colourless oil (23 mg, 0.068 mmol, 34%); $[\alpha]_D^{20}$ = +42.6 (*c* 0.50, $CHCl_3$); Chiral HPLC analysis, Chiralpak ID (95:5 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*,5*R*): 20.2 min, t_R(2*R*,5*R*): 22.4 min, >99:1 er; ν_{max} (thin film, $CHCl_3$) 1751 (C═O), 1375 (C—N), 1175 (Ar—SO_2N); 1089 (C—O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 1.48 (3H, d, *J* 6.7, C(5)CH_3), 2.40 (3H, s, ArCH_3), 4.49 (1H, qd, *J* 6.7, 1.3, C(5)*H*), 6.39 (1H, d, *J* 1.3, C(2)*H*Ph), 7.14–7.16 (2H, m, N(3)SO_2Ar*C*(3,5)*H*), 7.29–7.40 (4H, m, C(2)Ar*C*(2,3,5,6)*H*), 7.41–7.49 (3H, m, N(3)SO_2Ar*C*(2,6)*H*+C(2)Ar*C*(4)*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 17.2 (C(5)CH_3), 21.8 (ArCH_3), 74.4 (*C*(5)H), 90.8 (*C*(2)H), 128.1 (C(2)Ar*C*(3,5)H), 128.4 (N(3)SO_2-Ar*C*(2,6)H), 128.5 (C(2)Ar*C*(2,6)H), 129.6 (N(3)SO_2Ar*C*(3,5)H), 130.4 (C(2)Ar*C*(4)H), 135.3 (N(3)SO_2Ar*C*(1)), 136.3 (C(2)Ar*C*(1)), 145.5 (N(3)SO_2Ar*C*(4)), 170.9 (*C*(4)═O); HRMS (NSI$^+$) $C_{17}H_{18}NO_4S^+$ [M+H]$^+$ requires 332.0951, found 332.0953 (+0.6 ppm).

4.4.3. (2*R*,5*R*)-2-(3-Fluorophenyl)-5-methyl-3-tosyloxazolidin-4-one 23

Using general procedure 4.4—(3*R*)-2-tosyl-3-(3-fluorophenyl)-1,2-oxaziridine (3*R*)-**19** (175.8 mg, 0.6 mmol), 1-oxopropan-2-yl 4-nitrobenzoate **13** (45 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11**

(8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 2 CV, 100:0 to 90:10 10 CV, 90:10 3 CV)], the title compound **23** as a colourless oil (32 mg, 0.09 mmol, 46%); $[\alpha]_D^{20}$ = +31.5 (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (95:5 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 211 nm, 40 °C) t_R(2*R*,5*R*): 11.6 min, t_R(2*S*,5*S*): 21.6 min, 98.5:1.5 er; ν_{max} (thin film); 1751 (C═O), 1371 (C—N), 1187 (R-SO_2N), 1056, (C—O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 1.41 (3H, d, *J* 6.8 C(5)CH_3), 2.43 (3H, s, ArCH_3), 4.50 (1H, qd, *J* 6.8, 1.1, C(5)*H*CH_3), 6.51 (1H, d, *J* 1.1, C(2)*H*Ar), 6.95–6.98 (1H, m, C(2)Ar(2)*H*), 7.06–7.18 (2H, m, C(2)Ar(4,5)*H*), 7.20–7.30 (2H, m, N(3)SO_2Ar(3,5)*H*), 7.35 (1H, app. td, *J* 8.0, 5.6, C(2)Ar(6)*H*), 7.60–7.66 (2H, m, N(3)SO_2Ar(2,6)*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 16.9 (C(5)*C*H$_3$), 21.9 (Ar*C*H$_3$), 73.7 (*C*(5)H), 89.8 (*C*(2)H), 114.1 (d, $^2J_{C-F}$ 22.6, C(2)Ar*C*(2)H), 177.1 (d, $^2J_{C-F}$ 21.2, C(2)Ar*C*(4)H), 122.94 (d, $^4J_{C-F}$ 3.1, C(2)Ar*C*(6)H), 128.3 (N(3)SO_2Ar*C*(2,6)H), 129.7 (N(3)SO_2Ar*C*(3,5)H), 130.5 (d, $^3J_{C-F}$ 8.1 C(2)Ar*C*(5)H), 134.8 (N(3)SO_2Ar*C*(1)), 139.3 (d, $^3J_{C-F}$ 6.4, C(2)Ar*C*(1)), 146.0 (N(3)SO_2Ar*C*(4)H), 162.85 (d, $^1J_{C-F}$ 248.0, C(2)Ar*C*(3)F), 170.9 (*C*(4)═O). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F: −111.8; HRMS (NSI$^+$) $C_{17}H_{17}FNO_4S^+$ [M+H]$^+$ requires 350.0857, found 350.0859 (+0.6 ppm).

4.4.4. (2*R*,5*R*)-2-(4-Fluorophenyl)-5-methyl-3-tosyloxazolidin-4-one 24

Using general procedure 4.4—(3*R*)-2-tosyl-3-(4-fluorophenyl)-1,2-oxaziridine (3*R*)-**20** (175.8 mg, 0.6 mmol), 1-oxopropan-2-yl 4-nitrobenzoate **13** (45 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 2 CV, 100:0 to 90:10 10 CV, 90:10 3 CV)], the title compound **24** as a colourless oil (20 mg, 0.06 mmol, 28%); $[\alpha]_D^{20}$ = +24.4 (*c* 0.50, $CHCl_3$); Chiral HPLC analysis, Chiralpak IC (80:20 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 211 nm, 40 °C) t_R(2*R*,5*R*): 6.3 min, t_R(2*S*,5*S*): 7.5 min, >99:1 er; ν_{max} (thin film, $CHCl_3$) 1749 (C═O), 1371 (C—N), 1229 (C—F), 1172 (R-SO_2N), 1088 (C—O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 1.42 (3H, d, *J* 6.7, C(5)HCH_3), 2.43 (3H, s, ArCH_3), 4.52 (1H, qd, *J* 6.7, 1.1, C(5)*H*CH_3), 6.52 (1H, d, *J* 1.1 (C(2)*H*Ar), 7.02–7.06 (2H, app. t, *J* 8.6, C(2)Ar(3,5)*H*), 7.22–7.27 (2H, m, N(3)SO_2Ar(3,5)*H*), 7.28–7.34 (2H, m, C(2)Ar(2,6)*H*), 7.57–7.61 (2H, m, N(3)SO_2Ar(2,6)*H*). ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 17.0 (C(5)*C*H$_3$), 21.9 (Ar*C*H$_3$), 73.6 (*C*(5)H), 90.0 (*C*(2)H), 115.8 (d, $^2J_{C-F}$ 21.8, C(2)Ar*C*(3,5)H), 128.3 (N(3)SO_2-Ar*C*(2,6)H), 129.2 (d, $^3J_{C-F}$ 8.6, C(2)Ar*C*(2,6)H) 129.7 (N(3)SO_2Ar*C*(3,5)H), 132.9 (d, $^4J_{C-F}$ 3.4, C(2)Ar*C*(1)), 134.9 (N(3)SO_2Ar*C*(1)), 145.9 (N(3)SO_2Ar*C*(4)CH$_3$), 163.7 (d, $^1J_{C-F}$ 249.7, C(2)Ar*C*(4)F), 170.9 (*C*(4)═O). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F: −110.8; HRMS (NSI$^+$) $C_{17}H_{17}FNO_4S^+$ [M+H]$^+$ requires 350.0857, found 350.0859 (+0.6 ppm).

4.4.5. (2*R*,5*R*)-5-Methyl-2-(4-trifluoromethylphenyl)-3-tosyloxazolidin-4-one 25

Using general procedure 4.4—(3*R*)-2-tosyl-3-(4-(trifluoromethyl)phenyl)-1,2-oxaziridine (3*R*)-**21** (137 mg, 0.6 mmol), 1-oxopropan-2-yl 4-nitrobenzoate **13** (45 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 2 CV, 100:0 to 90:10 10 CV, 90:10 3 CV)], the title compound **25** as an off-white crystalline solid (32 mg, 0.08 mmol, 40%); mp 72–74 °C; $[\alpha]_D^{20}$ = +17.4 (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (95:5 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 201 nm, 40 °C) t_R(2*S*,5*S*): 5.3 min, t_R(2*R*,5*R*): 6.0 min, 97.5:2.5 er; ν_{max} (thin film, $CHCl_3$) 1753 (C═O), 1371 (C—N) 1188 (R-SO_2N), 1066 (C—O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 1.42 (3H, d, *J* 6.8, C(5)HCH_3), 2.42 (3H, s, ArCH_3), 4.52 (1H, qd, *J* 6.8, 1.1, C(5)*H*CH_3), 6.56 (1H, s, C(2)*H*Ar), 7.20–7.25 (2H, m, (C(2)Ar(2,6)H), 7.40–7.50 (2H, m, N(3)SO_2Ar(3,5)H), 7.54–7.65 (4H, d, *J* 6.6, C(2)Ar(3,5)H + N(3)SO_2Ar(2,6)H); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 16.8 (C(5)*C*H$_3$), 21.7 (Ar*C*H$_3$), 73.6 (*C*(5)H), 89.6 (*C*(2)H), 123.7 (q, $^1J_{C-F}$ 272.5, *C*F$_3$), 125.7 (q, $^3J_{C-F}$ 3.8, (C(2)Ar*C*(3,5)H), 127.5 (C(2)Ar*C*(2,6)H), 128.1 (N(3)SO_2Ar*C*(2,6)H), 129.6 (N(3)SO_2Ar*C*(3,5)H), 132.1 (q, $^2J_{C-F}$ 32.6, (C(2)Ar*C*(4)), 134.7 (N(3)SO_2ArC(1)), 140.6 (C(2)ArC(1)), 146.0 (N(3)SO_2ArC(4)), 170.6 (C(4)═O); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F: −62.8; HRMS (NSI$^+$) $C_{18}H_{17}F_3NO_4S^+$ [M+H]$^+$ requires 400.0825, found 400.0823 (-0.5 ppm).

4.4.6. (2*R*,5*R*)-5-Methyl-2-pentyl-3-tosyloxazolidin-4-one 26

Using general procedure 4.4—(3*R*)-3-pentyl-2-tosyl-1,2-oxaziridine (3*R*)-**22** (162 mg, 0.6 mmol), 1-oxopropan-2-yl 4-nitrobenzoate **13** (45 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 1 CV, 100:0 to 90:10 20 CV, 90:10 3 CV)], the title compound **26** as a transparent oil (40 mg, 0.12 mmol, 62%); $[\alpha]_D^{20}$ = +22.4 (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (98:2 hexane:*i*-PrOH, flow rate 1 mL min^{-1}, 201 nm, 30 °C) t_R(2*R*,5*R*): 16.2 min, t_R(2*S*,5*S*): 33.7 min, 94:6 er; ν_{max} (thin film, $CHCl_3$) 1739 (C═O), 1372 (C—N), 1168 (Ar—SO_2N); 1066 (C—O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 0.81–1.01 (3H, m, CH_2CH_3), 1.14–1.58 (9H, m, 3 × CH_2 + C(5)CH_3), 1.75–1.96 (1H, m, C(2)HC*H*^{a}H^b), 1.97–2.14 (1H, m, C(2)HCH^a*H*^{b}), 2.47 (3H, s, ArCH_3), 4.39 (1H, qd, *J* 6.7, 1.2, C(5)*H*CH$_3$), 5.66 (1H, ddd, *J* 7.9, 2.4, 1.2, C(2)*H*CH$_2$), 7.33–7.44 (2H, m, ArC(3,5)*H*), 7.78–8.16 (2H, m, ArC(2,6)*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 14.1 (CH_2CH_3), 17.2 (C(5)*C*H$_3$), 21.9 (Ar*C*H$_3$), 22.7 (*C*H$_2$), 23.6 (*C*H$_2$), 31.4 (*C*H$_2$), 35.5 (C(2)*C*H$_2$), 73.1 (*C*(5)H), 90.9 (*C*(2)H), 128.3 (Ar*C*(2,6)H), 129.9 (Ar*C*(3,5)H), 135.4 (ArC(1)), 145.8 (Ar*C*(4)CH$_3$), 171.2 (*C*(4)═O); Selected data for minor diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.20 (1H, qd, *J* 6.7, 0.9, C(5)*H*CH$_3$), 5.55 (1H, ddd, *J* 6.5, 2.0, 0.9, C(2)*H*CH$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 16.8 (C(5)*C*H$_3$), 35.6 (C(2)*C*H$_2$), 73.7 (*C*(5)H), 128.3 (N(3)SO_2Ar*C*(2,6)H); HRMS (NSI$^+$) $C_{16}H_{24}NO_4S^+$ [M+H]$^+$ requires 326.1421, found 326.1421 (+0.1 ppm).

4.4.7. (2*R*,5*R*)-5-Benzyl-2-phenyl-3-tosyloxazolidin-4-one 33

Using general procedure 4.4—(3*R*)-3-phenyl-2-tosyl-1,2-oxaziridine (3*R*)-**6** (165 mg, 0.6 mmol), 1-oxo-4-phenylbutan-2-yl 4-nitrobenzoate **27** (55 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 2 CV, 100:0 to 90:10 10 CV, 90:10 3 CV)], the title compound **33** as an off-white crystalline solid (36 mg, 0.088 mmol, 44%); mp 128–131 °C; $[\alpha]_D^{20}$ = +61.2 (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (99:1 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 201 nm, 40 °C) t_R(2*S*,5*S*): 33.4 min, t_R(2*R*,5*R*): 37.0 min, >99:1 er; ν_{max} (thin film, $CHCl_3$) 1751 (C═O), 1375 (C—N), 1175 (Ar—SO_2N); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.40 (3H, s, ArCH_3), 3.04 (1H, dd, *J* 14.5, 6.0, C(5)HCH_aH$_b$Ar), 3.14 (1H, dd, *J* 14.5, 4.4, C(5)HCH$_a$*H*$_b$Ar), 4.73 (1H, ddd, *J* 6.0, 4.4, 1.5, C(5)*H*), 6.21 (1H, d, *J* 1.5, C(2)*H*Ph), 7.12–7.27 (9H, m, N(3)SO_2Ar(3,5)*H* + C(2)Ar(2,6)*H* + 5 × CH_2Ar*H*), 7.30–7.35 (2H, m, C(2)Ar(3,5)*H*), 7.36–7.42 (1H, m, C(2)Ar(4)*H*), 7.42–48 (2H, m, N(3)SO_2Ar(2,6)*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 21.8 (Ar*C*H$_3$), 37.8 (C(5)*C*H$_2$Ph), 78.1 (*C*(5)H), 91.4 (*C*(2)H), 127.2 (CH_2Ar*C*(4)H), 127.3 (C(2)Ar*C*(2,6)H), 128.3 (N(3)SO_2Ar*C*(2,6)H), 128.6 (C(2)Ar*C*(3,5)H), 128.7 (CH_2-Ar*C*(3,5)H), 129.6 (N(3)SO_2Ar*C*(3,5)H), 129.8 (CH_2Ar*C*(2,6)H),

130.1 (C(2)ArC(4)H), 134.9 (N(3)SO_2ArC(1)), 135.2 (CH_2ArC(1)), 137.0 (C(2)ArC(1)), 145.5 (N(3)SO_2ArC(4)), 169.8 (C(4)=O); HRMS (APCI) $C_{23}H_{22}NO_4S$ [M+H] requires 408.1270, found 408.1272 (+0.5 ppm).

4.4.8. (2*R*,5*R*)-5-(4-Methoxybenzyl)-2-phenyl-3-tosyloxazolidin-4-one 34

Using general procedure 4.4—(3*R*)-3-phenyl-2-tosyl-1,2-oxaziridine (3*R*)-**6** (165 mg, 0.6 mmol), 1-(4-methoxyphenyl)-3-oxopropan-2-yl 4-nitrobenzoate **28** (66 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 1 CV, 100:0 to 85:15 20 CV, 85:15 3 CV)], the title compound **34** as a transparent oil (21 mg, 0.05 mmol, 24%). $[\alpha]_D^{20}$ = +60.6 (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralpak IC (80:20 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 211 nm, 40 °C) t_R(2*R*,5*R*): 10.1 min, t_R(2*S*,5*S*): 13.7 min, 99:1 er; ν_{max} (thin film) 1749 (C=O), 1371 (C—N), 1173 (R-SO_2N), 1090 (C—O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 2.41 (3H, s, ArCH_3), 3.00 (1H, dd, *J* 14.7, 5.6, C(5)HC$H_a$$H_b$Ar), 3.08 (1H, dd, *J* 14.7, 4.4, C(5)HC$H_a$$H_b$Ar), 3.80 (3H, s, OC$H_3$), 4.70 (1H, ddd, *J* 5.6, 4.4, 1.3, C(5)*H*C$H_a$$H_b$Ar), 6.22 (1H, d, *J* 1.3, C(2)*H*Ph), 6.76–6.77 (2H, m, CH_2ArC(3,5)*H*), 7.08–7.13 (2H, d, *J* 8.6, CH_2ArC(2,6)*H*), 7.13–7.18 (1H, m, N(3)SO_2ArC(3,5)*H*), 7.23–7.30 (2H, m, C(2)ArC(2,6)*H*), 7.30–7.35 (2H, m, C(2)ArC(3,5)*H*), 7.36–7.42 (1H, m, C(2)ArC(4)*H*), 7.42–7.46 (2H, m, N(3)SO_2ArC(2,6)*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 21.9 (ArCH_3), 36.9 (C(5)CH_2), 55.3 (ArOCH_3), 78.2 (*C*(5)*H*), 91.4 (*C*(2)H), 114.0 (CH_2ArC(3,5)H), 127.0 (CH_2ArC(1)), 127.3 (C(2)ArC(2,6)H), 128.3 (N(3)SO_2ArC(2,6)H), 128.7 (C(2)ArC(3,5)H), 129.5 (N(3)SO_2ArC(3,5)H), 130.1 (C(2)ArC(4)H), 130.9 (CH_2ArC(2,6)H), 134.9 (N(3)SO_2ArC(1)), 137.1 (C(2)ArC(1)), 145.5 (N(3)SO_2ArC(4)), 158.8 (CH_2ArC(4)), 169.9 (C(4)=O); HRMS (NSI$^+$) $C_{24}H_{24}NO_5S^+$ [M+H]$^+$ requires 438.1370, found 438.1369 (−0.2 ppm).

4.4.9. (2*R*,5*R*)-5-(Benzo[*d*][1,3]dioxol-5-ylmethyl)-2-phenyl-3-tosyloxazolidin-4-one 35

Using general procedure 4.4—(3*R*)-3-phenyl-2-tosyl-1,2-oxaziridine (3*R*)-**6** (165 mg, 0.6 mmol), 1-(benzo[*d*][1,3]dioxol-5-yl)-3-oxopropan-2-yl 4-nitrobenzoate **29** (69 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 1 CV, 100:0 to 93:7 20 CV, 93:7 5 CV, 93:7 to 90:10 12 CV)] to give the title compound **35** as a transparent oil (22 mg, 0.05 mmol, 24%); $[\alpha]_D^{20}$ = +124.0 (*c* 0.5, $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (95:5 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 201 nm, 40 °C) t_R(2*S*,5*S*): 16.1 min, t_R(2*R*,5*R*): 18.0 min, >99:1 er; ν_{max} (thin film, $CHCl_3$) 1749 (C=O), 1369 (C—N), 1173 (R-SO_2N), 1090 (C—O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 2.41 (3H, s, ArCH_3), 2.96 (1H, dd, *J* 14.7, 5.8, C(5)HC$H_a$$H_b$Ar), 3.06 (1H, dd, *J* 14.7, 4.3, C(5)HC$H_a$$H_b$Ar), 4.68 (1H, ddd, *J* 5.8, 4.3, 1.4, C(5)*H*C$H_a$$H_b$Ar), 5.92–5.95 (2H, m, ArOCH^aH^bOAr), 6.29 (1H, d, *J* 1.4, C(2)*H*Ph), 6.65 (1H, dd, *J* 7.9, 1.7, C(5)CH_2Ar(6)*H*), 6.67 (1H, d, *J* 7.9, C(5)CH_2Ar(5)*H*), 6.70 (1H, d, *J* 1.7, C(5)CH_2Ar(2)*H*), 7.13–7.19 (2H, m, N(3)SO_2Ar(3,5)*H*), 7.27–7.31 (2H, m, C(2)Ar(2,6)*H*), 7.31–7.36 (2H, m, C(2)Ar(3,5)*H*), 7.37–7.42 (1H, m, C(2)Ar(4)*H*), 7.44–7.51 (2H, m, N(3)SO_2Ar(2,6)*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 21.9 (ArCH_3), 37.4 (C(5)CH_2Ar), 78.1 (*C*(5)H), 91.3 (*C*(2)H), 101.0 (ArO*C*OAr), 108.4 (CH_2ArC(5)H), 110.1 (CH_2ArC(1)), 110.3 (CH_2ArC(2)H), 123.0 (CH_2ArC(6)H), 127.3 (C(2)ArC(2,6)H), 128.3 (N(3)SO_2ArC(2,6)H), 128.7 (CH_2ArC(3)), 128.8 (C(2)ArC(3,5)H), 129.5 (N(3)SO_2ArC(3,5)H), 129.5 (CH_2ArC(4)), 130.1 (C(2)ArC(4)H), 134.9 (N(3)SO_2ArC(1)), 137.1 (C(2)ArC(1)), 145.6 (N(3)SO_2ArC(4)), 169.7 (*C*(4)=O); HRMS (NSI$^+$) $C_{24}H_{22}NO_6S^+$ [M+H]$^+$ requires 452.1162, found 452.1162 (−0.1 ppm).

4.4.10. (2*R*,5*R*)-5-Butyl-2-phenyl-3-tosyloxazolidin-4-one 36

Using general procedure 4.4—(3*R*)-3-phenyl-2-tosyl-1,2-oxaziridine (3*R*)-**6** (165 mg, 0.6 mmol), 1-oxohexan-2-yl 4-nitrobenzoate **30** (55 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 1 CV, 100:0 to 80:20 20 CV, 80:20 3 CV)], the title compound **36** as a transparent oil (12 mg, 0.03 mmol, 16%); $[\alpha]_D^{20}$ = +51.4 (*c* 0.50, $CHCl_3$); Chiral HPLC analysis, Chiralpak IC (80:20 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 211 nm, 40 °C) t_R(2*R*,5*R*): 6.2 min, t_R(2*S*,5*S*): 6.6 min, >99:1 er; ν_{max} (thin film, $CHCl_3$) 1749 (C=O), 1373 (C—N), 1172 (R-SO_2N), 1090 (C—O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 0.86 (3H, t, *J* 7.1, CH_2CH_3), 1.20–1.34 (3H, m, C(5)HCH_2C$H_a$$H_b$-C$H_2CH_3$), 1.33–1.48 (1H, m, C(5)HCH_2C$H_a$$H_b$), 1.65–1.76 (1H, m, C(5)HC$H_a$$H_b$), 1.76–1.91 (1H, m, C(5)HC$H_a$$H_b$), 2.41 (3H, s, ArC$H_3$), 4.46 (1H, ddd, *J* 7.1, 4.4, 1.3, C(5)*H*CH_2), 6.52 (1H, d, *J* 1.3, C(2)*H*), 7.17–7.23 (2H, m N(3)SO_2ArC(3,5)*H*), 7.29–7.38 (4H, m, C(2)ArC(2,6)*H* + C(2)ArC(3,5)*H*), 7.37–7.47 (1H, m, C(2)ArC(4)*H*), 7.52–7.58 (2H, m, N(3)SO_2ArC(2,6)*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 14.0 ((CH_2)$_3$CH_3), 21.8 (ArCH_3), 22.5 (C(5)HCH_2CH_2CH_2CH_3), 26.6 (C(5)HCH_2CH_2CH_2CH_3), 31.4 (C(5)HCH_2CH_2CH_2CH_3), 77.4 (*C*(5)H), 91.1 (*C*(2)H), 127.2 (C(2)ArC(2,6)H), 128.3 (N(3)SO_2ArC(2,6)H), 128.8 (C(2)ArC(3,5)H), 129.6 (N(3)SO_2ArC(3,5)H), 130.1 (C(2)ArC(4)H), 135.0 (N(3)SO_2ArC(1)), 137.1 (C(2)ArC(1)), 145.7 (N(3)SO_2-ArC(4)), 170.8 (*C*(4)=O); HRMS (NSI$^+$) $C_{20}H_{24}NO_4S^+$ [M+H]$^+$ requires 374.1421, found 374.1422 (+0.4 ppm).

4.4.11. (2*R*,5*R*)-5-(2-(Benzyloxy)ethyl)-2-phenyl-3-tosyloxazolidin-4-one 37

Using general procedure 4.4—(3*R*)-3-phenyl-2-tosyl-1,2-oxaziridine (3*R*)-**6** (165 mg, 0.6 mmol), 4-(benzyloxy)-1-oxobutan-2-yl 4-nitrobenzoate **31** (69 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 1 CV, 100:0 to 80:20 20 CV, 80:20 3 CV)] to give the title compound **37** as a transparent oil (13 mg, 0.03 mmol, 14%). $[\alpha]_D^{20}$ = +47.6 (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralpak IC (80:20 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 211 nm, 40 °C) t_R(2*R*,5*R*): 10.1 min, t_R(2*S*,5*S*): 12.4 min, >99:1 er; ν_{max} (thin film) 1751 (C=O), 1371 (C—N), 1173 (R-SO_2N), 1088 (C—O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.02 (1H, dddd, *J* 14.5, 7.4, 6.4, 5.3, C(5)HCH_a-H_bCH_2OBn), 2.15 (1H, dddd, *J* 14.5, 7.2, 5.6, 4.6, C(5)HC$H_a$$H_bCH_2$), 2.39 (3H, s, ArC$H_3$), 3.52–3.70 (2H, m, C$H_2$OBn), 4.45 (2H, s, OC$H_2$-Ph), 4.65 (1H, ddd, *J* 7.4, 4.6, 1.3, C(5)*H*), 6.50 (1H, d, *J* 1.3, C(2)*H*), 7.15–7.21 (2H, m, N(3)SO_2ArC(3,5)*H*), 7.23–7.38 (9H, m, Ar*H*), 7.39–7.47 (1H, m, Ar*H*), 7.50–7.56 (2H, m, N(3)SO_2ArC(2,6)*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 21.8 (ArCH_3), 31.8 (C(5)CH_2), 65.0 (CH_2-OBn), 73.1 (OCH_2Ph), 74.6 (*C*(5)H), 91.2 (*C*(2)H), 127.3 (C(2)ArC(2,6)H), 127.8 (OCH_2ArC(4)H), 127.9 (OCH_2ArC(2,6)H), 128.3 (N(3)SO_2ArC(2,6)H), 128.5 (OCH_2ArC(3,5)H), 128.8 (C(2)ArC(3,5)H), 129.6 (N(3)SO_2ArC(3,5)H), 130.1 (C(2)ArC(4)H), 135.0 (N(3)SO_2-ArC(1)), 137.0 (C(4)ArC(1)), 138.2 (OCH_2ArC(1)), 145.6 (N(3)SO_2-ArC(4)), 170.7 (*C*(4)=O); HRMS (NSI$^+$) $C_{25}H_{26}NO_5S^+$ [M+H]$^+$ requires 452.1532, found 452.1531 (−0.2 ppm).

4.4.12. 2-(2-((2*R*,5*R*)-4-Oxo-2-phenyl-3-tosyloxazolidin-5-yl)ethyl)isoindoline-1,3-dione 38

Using general procedure 4.4—(3*R*)-3-phenyl-2-tosyl-1,2-oxaziridine (3*R*)-**6** (165 mg, 0.6 mmol), 4-(1,3-dioxoisoindolin-2-yl)-1-oxobutan-2-yl 4-nitrobenzoate **32** (76 mg, 0.2 mmol), cesium

carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.4 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (90:10 1 CV, 90:10 to 75:25 15 CV, 75:25 6 CV)], the title compound **38** as a transparent oil (24 mg, 0.05 mmol, 24%). $[\alpha]_D^{20}$ = +31.0 (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralpak IB (90:10 hexane:*i*-PrOH, flow rate 1 mL min^{-1}, 211 nm, 40 °C) t_R(2*S*,5*S*): 31.9 min, t_R(2*R*,5*R*): 42.0 min, >99:1 er; ν_{max} (thin film, $CHCl_3$) 1749 (C═O), 1712 (C═O), 1373 (C—N), 1175 (R-SO_2N), 1090 (C—O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.07–2.26 (2H, m, C(5)CH_2), 2.39 (3H, s, ArCH_3), 3.68–3.80 (1H, m, NC$H_a$$H_b$), 3.83–3.95 (1H, m, NC$H_a$$H_b$), 4.53 (1H, ddd, *J* 7.6, 4.2, 1.2, C(5)*H*), 6.53 (1H, d, *J* 1.2, C(2)*H*Ph), 7.15–7.21 (2H, m, N(3)SO_2ArC(3,5)*H*), 7.22–7.27 (2H, m, C(2)ArC(2,6)*H*), 7.28–7.39 (2H, m, C(2)ArC(3,5)*H*), 7.37–7.43 (1H, m, C(2)ArC(4)*H*), 7.51–7.57 (2H, m, N(3)SO_2ArC(2,6)*H*), 7.70 (2H, m, PhthC(5,6)*H*), 7.82 (2H, m, PhthC(4,7)*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 21.8 (C(5)CH_2), 30.2 (ArCH_3), 34.1 (CH_2N), 75.4 (*C*(5)H), 91.1 (*C*(2)H), 123.5 (PhthC(4,7)H), 127.1 (C(2)Ar*C*(2,6)H), 128.8 (N(3)SO_2Ar*C*(2,6)H), 128.8 (C(2)Ar*C*(3,5)H), 129.6 (N(3)SO_2Ar*C*(3,5)H), 130.1 (C(2)Ar*C*(4)H), 132.2 (Phth*C*(3a,7a)), 134.1 (Phth*C*(5,6)H), 134.8 (N(3)SO_2Ar*C*(1)), 136.7 (C(2)Ar*C*(1)), 145.7 (N(3)SO_2Ar*C*(4)), 168.3 (Phth*C*(1,3)═O), 169.6 (*C*(4)═O); HRMS (NSI$^+$) $C_{26}H_{26}N_3O_6S^+$ $[M+NH_4]^+$ requires 508.1537, found 508.1529 (−1.5 ppm).

4.4.13. (2*R*,9b*S*)-2,9b-Dimethyl-9b*H*-benzo[4,5]isothiazolo[3,2-*b*]oxazol-3(2*H*)-one 5,5-dioxide 40

Using general procedure 4.4—7b-methyl-7b*H*-benzo[*d*][1,2]oxazireno[2,3-*b*]isothiazole 3,3-dioxide (±)-**39** (118 mg, 0.6 mmol), 1-oxopropan-2-yl 4-nitrobenzoate **13** (45 mg, 0.2 mmol), cesium carbonate (71.5 mg, 0.22 mmol), N-heterocyclic carbene precatalyst **11** (8.38 mg, 0.02 mmol) in anhydrous 1,4-dioxane (4 mL) gave, after purification by Biotage® Isolera™ 4 [SNAP Ultra 10 g, 36 mL min^{-1}, hexane:EtOAc (100:0 1 CV, 100:0 to 90:10 20 CV, 90:10 3 CV)], the title compound **40** as a transparent oil (10 mg, 0.12 mmol, 20%). $[\alpha]_D^{20}$ = +35.0 (*c* 0.20, $CHCl_3$); Chiral HPLC analysis, Chiralcel OD-H (98:2 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 201 nm, 40 °C) t_R(2*R*,9b*S*): 24.6 min, t_R(2*S*,9b*R*): 53.9 min, 88:12 er; ν_{max} (thin film) 1765 (C═O), 1352 (C—N), 1184 (R-SO_2N); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 1.41 (3H, d, *J* 6.8, C(2)HCH_3), 1.96 (3H, s, C(9b)CH_3), 4.74 (1H, q, *J* 6.8, C(2)*H*CH_3), 7.62 (1H, app. d, *J* 7.8, C(9)*H*), 7.67 (1H, app. td, *J* 7.7, 1.0, C(7)*H*), 7.73–7.82 (2H, m, C(6,8)*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 16.6 (C(2)CH_3), 26.5 (C(9b)CH_3), 75.5 (*C*(2)H), 96.1 (*C*(9b)), 121.8 (Ar*C*(6)H), 123.6 (Ar*C*(9)H), 131.6 (Ar*C*(7)H), 134.6 (Ar*C*(8)H), 135.7 (Ar*C*(5a)), 139.5 (Ar*C*(9a)), 170.8 (C═O); HRMS (ESI$^+$) $C_{11}H_{11}NO_4SNa^+$ $[M+Na]^+$ requires 276.0301, found 276.0296 (−1.8 ppm).

4.4.14. (2*R*,5*R*)-5-Methyl-2-phenyloxazolidin-4-one 41

Anhydrous THF was sparged with argon for 30 mins, and then 1.3 mL transferred to a flame-dried Schlenk flask containing (2*R*,5*R*)-5-methyl-2-phenyl-3-tosyloxazolidin-4-one **14** (43 mg, 0.13 mmol). The flask was cooled to −78 °C and SmI_2 (2.6 mL, ~0.1 M in anhydrous THF, 0.26 mmol, 2 equiv) was added dropwise. The blue solution was warmed to rt and monitored by TLC. After 15 min the solution turned yellow and the reaction was diluted with EtOAc (20 mL) and washed with aq satd NH_4Cl (20 mL) and brine (20 mL). The organic fraction was dried ($MgSO_4$), filtered and concentrated under vacuum to give the title compound **41** as a colourless oil in accordance with literature[29] (13 mg, 0.07 mmol, 57%); $[\alpha]_D^{20}$ = −6.8 (*c* 1.00, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (95:5 hexane:*i*-PrOH, flow rate 1.5 mL min^{-1}, 211 nm, 40 °C) t_R(2*S*,5*S*): 7.0 min, t_R(2*R*,5*R*): 8.7 min >99:1 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 1.48 (3H, d, *J* 6.8, C(5)HCH_3), 4.54 (1H, qd, *J* 6.8, 2.1, C(5)*H*), 6.45 (1H, d, *J* 2.1, C(2)*H*), 7.10 (1H, br. s, N(3)*H*), 7.39–7.44 (5H, m, Ar*H*).

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A. Supplementary data[30]

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetasy.2016.10.012.

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