Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 4205

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**PAPER**

# Organic base effects in NHC promoted *O*- to *C*-carboxyl transfer; chemoselectivity profiles, mechanistic studies and domino catalysis†

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***Received 28th January 2011, Accepted 28th February 2011***
**DOI: 10.1039/c1ob05160a**

The *O*- to *C*-carboxyl transfer of oxazolyl carbonates promoted by triazolinylidenes, generated *in situ* with $NEt_3$, shows a markedly different rate and chemoselectivity profile to the same reaction promoted by triazolinylidenes generated using KHMDS. The mechanism of these pathways has been probed through extensive crossover studies to understand this process. The use of $NEt_3$ as a base allows domino multi-step reaction sequences to be developed, although chiral NHCs only generate modest levels of asymmetric induction (<15% ee) in these domino reaction processes.

## Introduction

N-Heterocyclic carbene (NHC) mediated catalysis has developed rapidly within the last decade to include a range of synthetic transformations that encompass both organometallic chemistry[1] and organocatalysis.[2,3] Significant advances in organocatalytic strategies employing NHCs have been made in recent years, through the development of a series of efficient umpolung,[4] conjugate umpolung[5] and redox strategies,[6] among a number of others.[7] An alternative reaction manifold, employing the ability of NHCs to act as Lewis base or nucleophilic catalysts has also been established. In this arena, Smith *et al.* first described the stoichiometric transfer of an alkoxycarbonyl unit from a 2-alkoxycarbonylimidazolium salt to benzyl alcohol in the presence of DABCO in 1994.[8] Building upon this work, Nolan and Hedrick independently showed that NHCs catalyse transesterification processes,[9] which has been extended to allow the kinetic resolution of alcohols with chiral NHCs.[10] Movassaghi and co-workers have also demonstrated that NHCs effectively catalyse the amidation of esters with amino alcohols, although an alternative mechanism involving the NHC acting as a Brønsted base, resulting in nucleophilic activation of the alcohol for an initial transesterification event, followed by rapid *O*- to *N*-acyl transfer, has been proposed.[11,12] Alternatively, Ye and co-workers,[13] and ourselves,[14] have recently developed a range of NHC-catalysed asymmetric transformations that harness the use of azolium enolates, formed from NHC addition to ketenes, for a number of formal cycloaddition and other processes.

As part of a programme of research concerned with developing Lewis-base[15] catalysed reactions,[16] we have previously shown that triazolinylidenes, generated by deprotonation of the corresponding triazolium salt **2** with a metallated base (typically KHMDS) can efficiently promote the Steglich rearrangement[17,18] of oxazolyl carbonates, a reaction process tolerant of a range of C(4)-substituents as well as alkyl and aryl carbonates (Fig. 1).[19] Cognisant of the elegant work of both Bode *et al.*[20] and Glorious *et al.*[21] concerning the nature of the base used to generate the NHC and the divergent fate of homoenolate reactions, we chose to investigate fully the effect of changing the base from an organometallic base to a weaker organic or inorganic base in this rearrangement process. Herein we demonstrate that the choice of base used to mediate the *O*- to *C*-carboxyl transfer promoted by NHCs affects both the rate of product formation and the chemoselectivity of this transformation. Additionally, the use of an organic base allows the inclusion of this *O*- to *C*-carboxyl

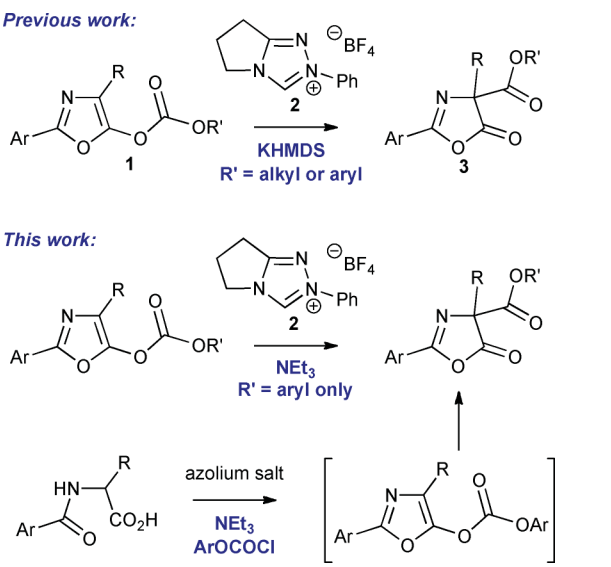


**Fig. 1** NHC-mediated *O*- to *C*-carboxyl transfer of oxazolyl carbonates.

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† Electronic supplementary information (ESI) available: All spectroscopic data for novel compounds. CCDC reference numbers 809724–809726. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob05160a

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transfer process into domino multi-step reaction sequences for the synthesis of *C*-carboxyazlactones.[22,23] Part of this work has been communicated previously.[24]

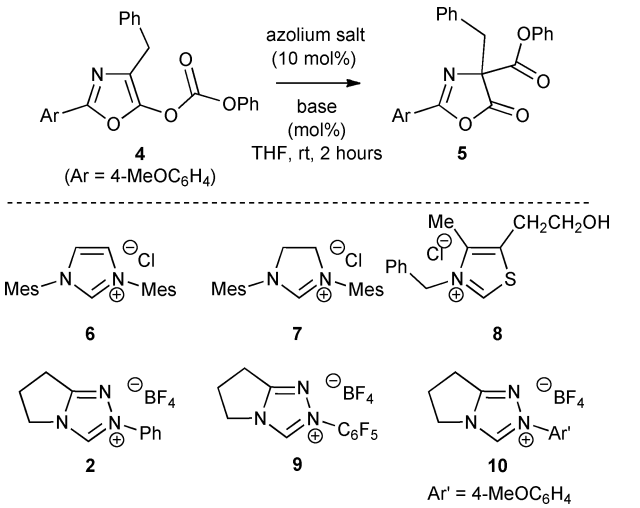
## Results and discussion

### Base effects upon NHC-mediated *O*- to *C*-carboxyl transfer of oxazolyl carbonates; reaction rates and chemoselectivity

Initial studies concentrated upon the use of $NEt_3$ as an organic base for the *O*- to *C*-carboxyl transfer rearrangement protocol. As our previous work has shown that oxazolyl phenyl carbonates undergo facile NHC promoted *O*- to *C*-carboxyl transfer, the rearrangement of phenyl carbonate **4** to **5** was chosen for optimization. Addition of $NEt_3$ (9 mol%) to a range of azolium salts (10 mol%) and subsequent rearrangement was investigated (Table 1). Employing the imidazolium, imidazolinium or thiazolium salts **6–8** returned only starting material even upon extended reaction times (entries 1–3), although triazolium precatalyst **2** gave complete conversion to **5** in THF within 2 h, giving **5** in 82% isolated yield (entry 4). The rate of rearrangement of **4** to **5** employing $NEt_3$ as the base with precatalyst **2** is notably slowed in comparison to the use of KHMDS for the same transformation, which proceeds to completion within 5 min at significantly lower catalyst loadings (typically <1 mol%).[19a,b] These disparate rates were initially proposed to correspond to the concentration of active NHC generated in these protocols, with KHMDS effecting quantitative conversion of salt **2** to the corresponding NHC, and $NEt_3$ generating an equilibrium concentration of the NHC necessary to promote rearrangement. In support of this hypothesis, increasing the stoichiometry of $NEt_3$ to 100 mol% resulted in a marked increase in reaction rate, giving complete conversion to **5** within 5 min (entry 5). Furthermore, doping of the reaction with $NEt_3$·HCl (1 eq) prior to addition of $NEt_3$ resulted in a decrease in the rate of rearrangement, proceeding to only 75% conversion to **5** after 2 h. Control experiments showed that neither $NEt_3$ nor triazolium salt **2** alone promote the rearrangement of **4** to **5** (entries 6 and 7), consistent with the need for *in situ* NHC generation to promote the desired *O*- to *C*-carboxyl transfer. DBU, proton sponge, $K_2CO_3$ and $Cs_2CO_3$ can also be used successfully with triazolium salt **2** in this process (entries 8–11) although DABCO, 2,6-lutidine or *N*-methylmorpholine promoted no rearrangement. Further catalyst screening showed that *N*-aryl triazolium salts **9** and **10** bearing either electron withdrawing or electron donating substituents also proved competent precatalysts for the rearrangement using $NEt_3$ (entries 12 and 13).[25]

The generality of the $NEt_3$ promoted process in combination with precatalyst **2** was next established. Intriguingly, variation of the carbonate functionality showed that rearrangement under these reaction conditions is highly chemoselective. Only aryl oxazolyl carbonates rearrange to their *C*-carboxyazlactones using $NEt_3$ as the base, with alkyl oxazolyl carbonates **11–13** inert to these reaction conditions, returning only starting materials even after extended reaction times (Table 2). $NEt_3$ can also be used to promote the rearrangement of 1-naphthyl oxazolyl carbonate **14** as well as aryl oxazolyl carbonates **15** and **16** incorporating electron withdrawing and electron donating substituents (entries

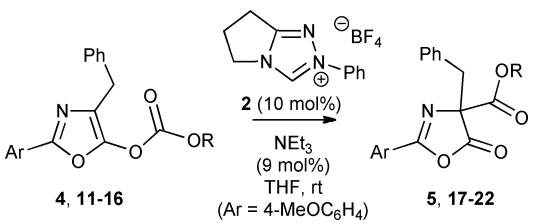
**Table 1** Organic base promoted NHC-catalysed *O*- to *C*-carboxyl transfer




| entry | salt | base (mol%) | product conversion[a] |
|---|---|---|---|
| 1 | **6** | $NEt_3$ (9) | 0% |
| 2 | **7** | $NEt_3$ (9) | 0% |
| 3 | **8** | $NEt_3$ (9) | 0% |
| 4 | **2** | $NEt_3$ (9) | >95% (82%)[b] |
| 5 | **2** | $NEt_3$ (100) | >95% (82%)[b,c] |
| 6 | — | $NEt_3$ (9) | 0% |
| 7 | **2** | — | 0% |
| 8 | **2** | DBU (9) | >90% |
| 9 | **2** | $K_2CO_3$ (9) | >95% |
| 10 | **2** | Proton sponge (9) | >95% |
| 11 | **2** | $Cs_2CO_3$ (9) | >95% |
| 12 | **9** | $NEt_3$ (9) | >95% |
| 13 | **10** | $NEt_3$ (9) | >95% |

[a] All reaction conversions were judged by $^1$H NMR spectroscopic analysis of the crude reaction product. [b] Isolated yield of homogeneous product after chromatographic purification. [c] Reaction time 5 min.

**Table 2** Chemoselective $NEt_3$ promoted NHC-catalysed *O*- to *C*-carboxyl transfer




| entry | oxazolyl carbonate | R | ester | product conversion[a] | Yield[b] |
|---|---|---|---|---|---|
| 1 | **4** | Ph | **5** | >95% | 82% |
| 2 | **11** | Me | **17** | 0% | — |
| 3 | **12** | Bn | **18** | 0% | — |
| 4 | **13** | $C(Me)_2CCl_3$ | **19** | 0% | — |
| 5 | **14** | 1-naphthyl | **20** | >95% | 85% |
| 6[c] | **15** | 4-$MeOC_6H_4$ | **21** | >95%[26] | 40% |
| 7[c] | **16** | 4-$FC_6H_4$ | **22** | >90%[26] | 31% |

[a] All reaction conversions were judged by $^1$H NMR spectroscopic analysis of the crude reaction product after two hours. [b] Isolated yield of homogeneous product after chromatographic purification. [c] Reaction conditions **2** (10 mol%), $NEt_3$ (100 mol%), THF (0.86 M), rt, 2 h.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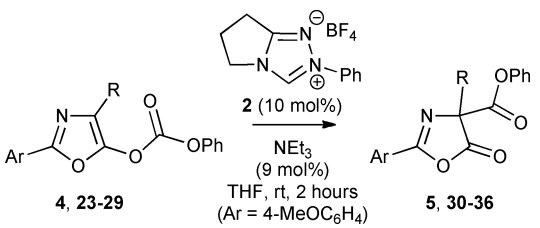
5–7).[26] Importantly, these observations contrast our previous work using KHMDS as the base with precatalyst **2**, which promotes carboxyl transfer for both aryl and alkyl oxazolyl carbonates. While a change in concentration of the active NHC in these reactions may account for the disparate rates of reaction observed within the $NEt_3$ or KHMDS promoted processes, the change in chemoselectivity of this reaction is intriguing. We investigated the possibility that $KBF_4$, generated *in situ* by deprotonation of triazolium salt **2** with KHMDS, may act as a mild co-operative Lewis-acid co-catalyst and aid this rearrangement process. To test this hypothesis, the formation of *C*-carboxyl **5** from **4** using $NEt_3$ (9 mol%) and triazolium salt **2** (10 mol%) in the presence of $KBF_4$ (1 eq) was monitored, resulting in a marked increase in reaction rate, giving >95% conversion after 60 min. However, methyl oxazolyl carbonate **11** did not rearrange under these conditions, consistent with the chemoselectivity of this process being unaffected by addition of $KBF_4$.

The generality of the $NEt_3$ promoted reaction protocol was investigated through variation of the C(4) substituent of the oxazolyl carbonate. A range of C(4)-alkyl (R = Me, Et, *n*-Bu, *i*-Bu, $CH_2CH_2SMe$, 4-$PhOCO_2C_6H_4CH_2$) and C(4)-aryl (R = Ph) phenyl oxazolyl carbonates readily rearrange to their *C*-carboxyl products (Table 3, entries 1–7). However, structurally challenging oxazolyl carbonates, such as those bearing a C(4)-α-branched *i*-Pr group that rearrange in good yield to the *C*-carboxyl product using KHMDS and precatalyst **2**, gave only low conversion to product (<15%), even with excess $NEt_3$.

**Table 3** Scope and limitations of the $NEt_3$ promoted NHC-catalysed *O*- to *C*-carboxyl transfer

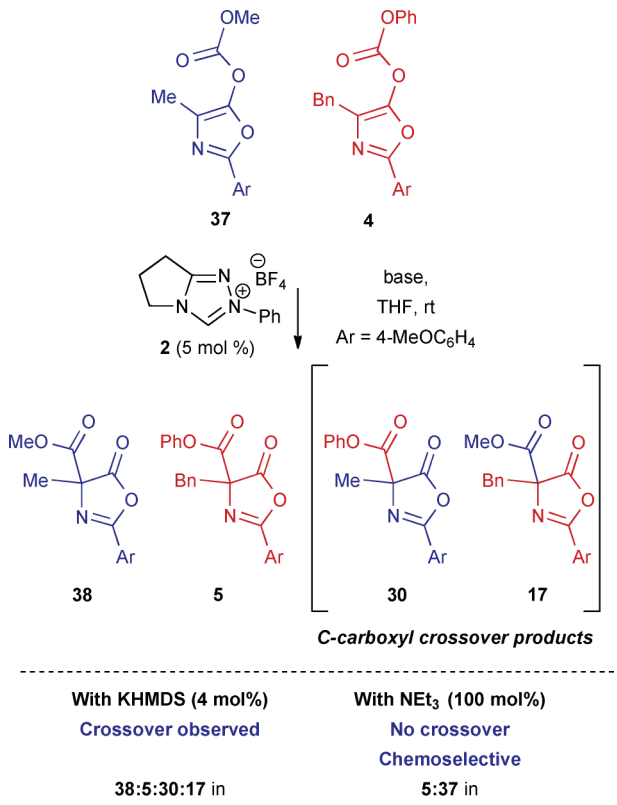



| entry | oxazolyl carbonate | R | ester | product conversion[a] | Yield[b] |
|---|---|---|---|---|---|
| 1 | **4** | Bn | **5** | >95% | 82% |
| 2 | **23** | Me | **30** | >95% | 81% |
| 3 | **24** | *n*-Bu | **31** | >95% | 81% |
| 4 | **25** | *i*-Bu | **32** | >95% | 78% |
| 5 | **26** | Ph | **33** | >95% | 72% |
| 6 | **27** | 4-$PhOCO_2C_6H_4CH_2$ | **34** | >90% | 77% |
| 7 | **28** | $CH_2CH_2SMe$ | **35** | >90% | — |
| 8 | **29** | *i*-Pr | **36** | <15% | — |

[a] All reaction conversions were judged by $^1$H NMR spectroscopic analysis of the crude reaction product. [b] Isolated yield of homogeneous product after chromatographic purification.

### Mechanistic studies: crossover experiments

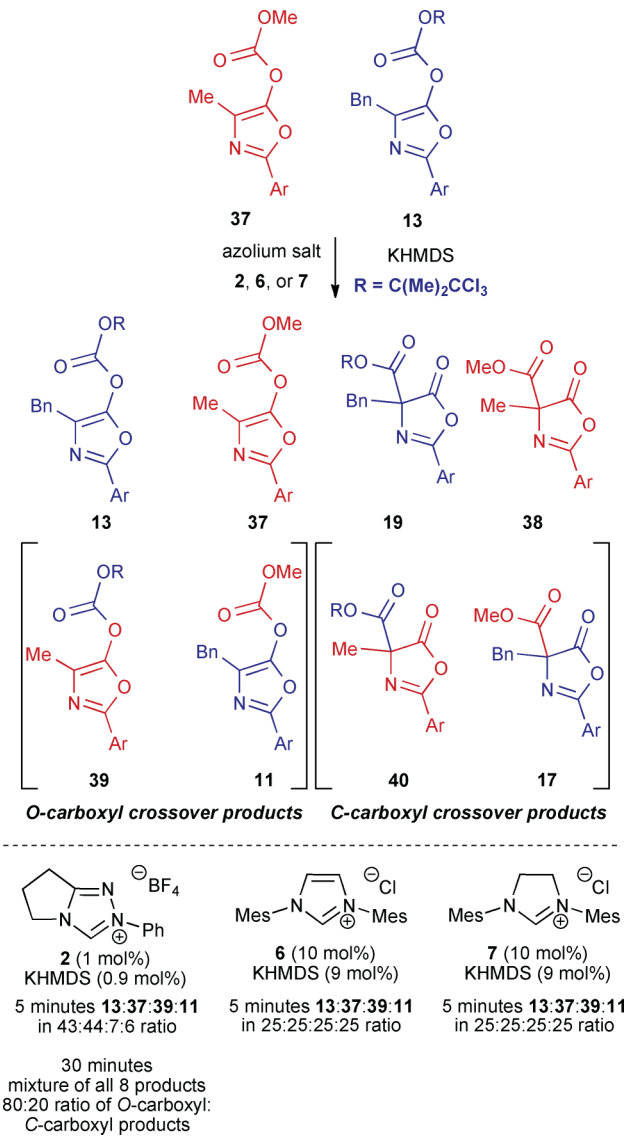
The notable differences in reactivity observed in this *O*- to *C*-carboxyl transfer process with a change in base from KHMDS to $NEt_3$ led us to fundamentally question the reaction mechanisms and reversibility of these processes, which we decided to probe by analysis of the product distributions arising from crossover experiments. In addition, we sought to clarify why the NHC derived from triazolium salt **2** is a better catalyst for this transformation than those derived from imidazolium or imidazolinium salts **6** and **7** using either $NEt_3$ or KHMDS as the base. Initial crossover studies showed that treatment of triazolium precatalyst **2** (5 mol%) with KHMDS (4 mol%) and subsequent addition of a 50 : 50 mixture of oxazolyl carbonates **4** and **37** gave, after 5 min and at complete reaction conversion, a 23 : 28 : 27 : 23 mixture of the four possible rearrangement products **38**, **5**, **30** and **17** respectively (Scheme 1).[27] However, treatment of a 50 : 50 mixture of oxazolyl carbonates **4** and **37** with precatalyst **2** and $NEt_3$ (1 eq) either in the presence or absence of $KBF_4$ (1 eq) gave, again after 5 min and at complete conversion of **4**, exclusively **5** and carbonate **37**. Further experiments showed that treatment of a 50 : 50 mixture of either *C*-carboxyl **4** and *O*-carboxyl **38**, or a 50 : 50 mixture of *C*-carboxyl **5** and **38**, with the NHC derived from KHMDS and precatalyst **2** both returned **5** and **38** exclusively, consistent with the C–C bond forming step in this transformation being irreversible.




**Scheme 1** NHC-catalysed *O*- to *C*-carboxyl transfer: crossover experiments.

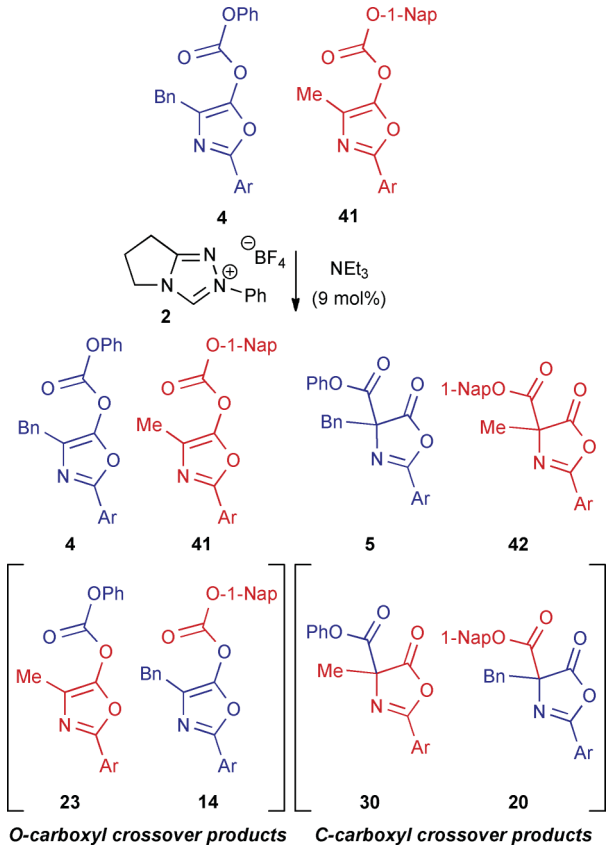
The generation of a near statistical product distribution upon rearrangement of the mixture of oxazolyl carbonates **4** and **37** with KHMDS is consistent with an intermolecular step occurring at some stage within this process. Further experiments were designed to distinguish between the possibility of crossover occurring in a pre-equilibrium first stage, resulting in scrambling of the 50 : 50 mixture of oxazolyl carbonates, and/or an intermolecular pathway between the enolate and a putative carboxyl transfer intermediate. Monitoring the product distribution formed upon treatment of a 50 : 50 mixture of oxazolyl carbonates **13** and **37**

with precatalyst **2** (1 mol%) and KHMDS (0.9 mol%) gave, after 5 min, a 43 : 44 : 7 : 6 ratio of exclusively *O*-carboxyl products **13** : **37** : **39** : **11**, that after 30 min gave a mixture of all eight possible *O*- and *C*-carboxyl products in a combined 80 : 20 ratio (Scheme 2). This product distribution is consistent with an initial reversible *O*-transcarboxylation process, followed by a relatively slow *C*-carboxylation event. Interestingly, treatment of a 50 : 50 mixture of **13** and **37** with imidazolium or imidazolinium salts **6** and **7** (10 mol%) respectively and KHMDS (9 mol%) resulted in rapid *O*-transcarboxylation to form an equimolar ratio of all four possible *O*-carboxyl products **13** : **37** : **39** : **11**, with no subsequent formation of any *C*-carboxyl products, even after extended reaction times. This is consistent with the nature of the *C*-carboxyl intermediate having a dominant effect upon the viability of the *C*-carboxylation process.




**Scheme 2** NHC-catalysed *O*- to *C*-carboxyl transfer: crossover experiments with triazolium, imidazolinium and imiadazolium precatalysts using KHMDS.

To probe the $NEt_3$ catalysed reaction pathway, the rearrangement of a 50 : 50 mixture of aryl oxazolyl carbonates **4** and **41** was monitored (Scheme 3). Using precatalyst **2** (10 mol%) and $NEt_3$ (9 mol%) a 25 : 25 : 25 : 25 mixture of *C*-carboxyl products **5** : **20** : **30** : **42** was observed after 5 min. Adjustment of the reaction conditions showed that using lower loadings of precatalyst **2** (1 mol%) and $NEt_3$ (0.9 mol%) [2 mM concentration] gave a mixture of all eight products (arising from *O*- and *C*-carboxyl transfer processes), again consistent with initial rapid transcarboxylation to generate a mixture of carbonates, with subsequent rearrangement to give a mixture of *C*-carboxyl products.




**Scheme 3** NHC-catalysed *O*- to *C*-carboxyl transfer: crossover experiments using $NEt_3$.

Taken together, these crossover experiments are consistent with both KHMDS and $NEt_3$ catalysed *O*- to *C*-carboxyl transfer processes proceeding through a similar mechanistic pathway, involving an initial reversible *O*-carboxylation process, followed by an irreversible *C*-carboxylation event (Fig. 2). This mechanistic scheme is consistent with previous crossover studies from Fu using a planar chiral PPY derivative as an asymmetric catalyst for this reaction. This mechanistic proposal does not, however, account for the difference in chemoselectivity noted within this NHC catalysed process using either KHMDS or $NEt_3$. As Alder and co-workers have shown that metallated bases such as KHMDS form complexes with NHCs,[28] it may be possible that metal complexation of the carbene upon deprotonation with a metallated base may lead to enhanced NHC reactivity in this reaction manifold. Alternatively, ion-pairing of a putative enolate intermediate with either an ammonium ($NEt_3H^+$) or $K^+$ counterion may give rise to the observed difference in reactivity in these systems; we are currently investigating the viability of these processes.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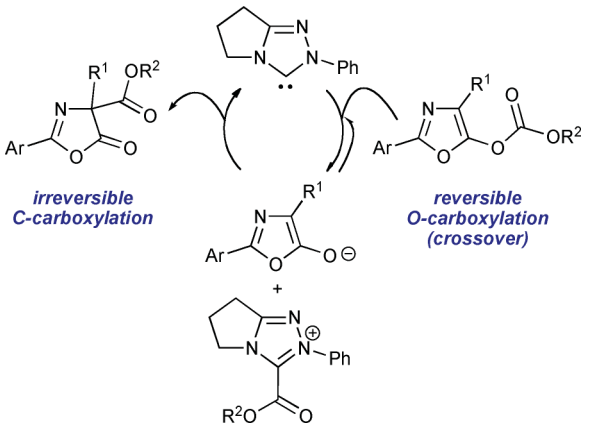



**Fig. 2** Postulated mechanism for the NHC-promoted *O*- to *C*-carboxyl transfer reaction.

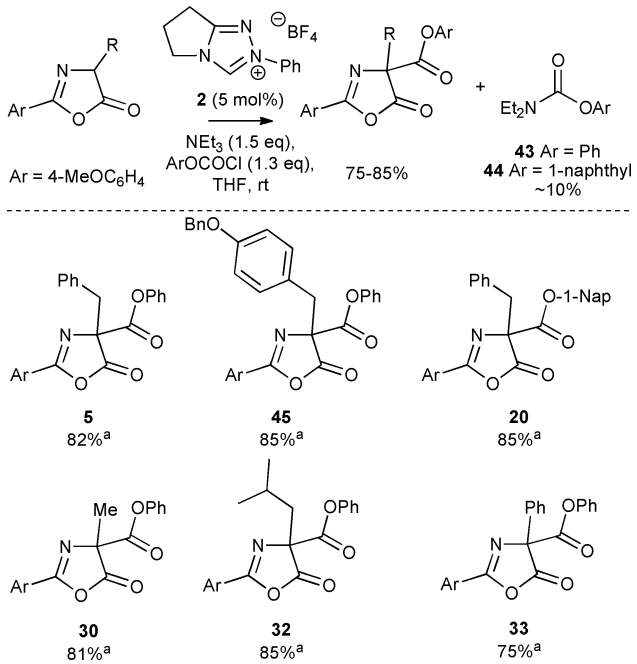
### Developing a domino two-step rearrangement protocol

Having validated the scope and limitations of employing $NEt_3$ as a base to promote the *O*- to *C*-carboxyl transfer process, the prospect of using $NEt_3$ to facilitate both the preparation of the oxazolyl carbonate[29] and the *in situ* generation of an NHC to promote a one-pot domino rearrangement protocol was investigated. The suitability of a variety of solvents to promote both oxazolyl carbonate formation from the corresponding azlactone, and the rearrangement with precatalyst **2** and $NEt_3$, were separately evaluated, with THF proving adequate for both stages of the proposed domino process. Extensive optimisation of this domino process showed that formation of *C*-carboxyl **5** from the parent azlactone required an excess of phenyl chloroformate and $NEt_3$, as competitive formation of phenyl diethylcarbamate **43** (prepared from dealkylation of triethylamine with the chloroformate)[30] inhibited the formation of the intermediate oxazolyl carbonate. A simple control experiment showed that excluding triazolium salt **2** from the reaction gave only oxazolyl carbonate **4** and carbamate **43**, again consistent with the need to generate an NHC *in situ* to promote *C*-carboxylation. The generality of this two-step domino process was established, with a range of azlactones giving their corresponding *C*-carboxyazlactones in 75–85% isolated yield after chromatographic purification using either phenyl or 1-naphthyl chloroformate (Scheme 4).[31,32]

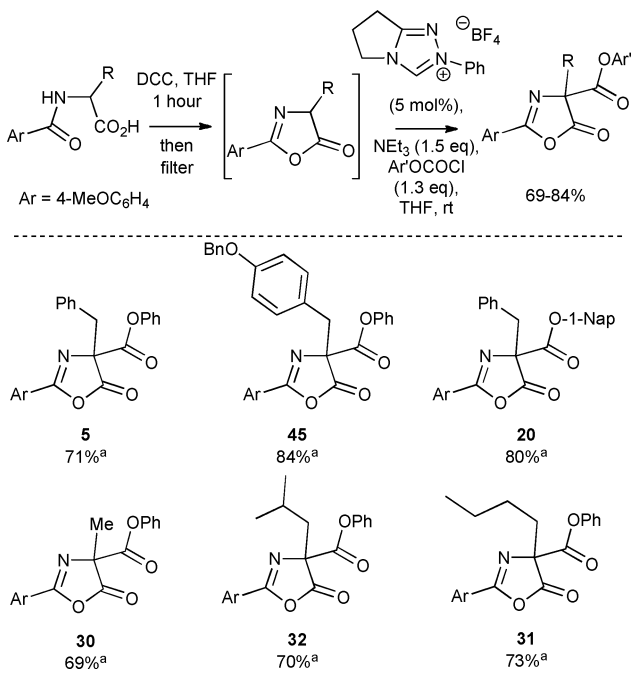
### Domino poly-step cyclisations

To further extend these domino reaction protocols, the ability to generate *C*-carboxyl products directly from *N*-*p*-anisoyl amino acids by incorporating a carboxylate activation and cyclisation step to generate azlactones *in situ*, was investigated. Treatment of *N*-*p*-anisoyl phenylalanine with DCC in THF,[33] followed by filtration of the urea by-product after 1 h, and sequential addition of triazolium salt **2** (5 mol%), $NEt_3$ (1.5 eq) and phenyl chloroformate (1.3 eq) gave *C*-carboxyl-**5** in 71% yield after chromatography. This simple process was applied to a number of derivatives, giving the desired *C*-carboxyazlactones in 69–84% isolated yields (Scheme 5).

As an alternative one-pot procedure for the direct preparation of *C*-carboxyazlactones from *N*-*p*-anisoyl amino acids,[34] the use of an aryl chloroformate to both promote their cyclisation and



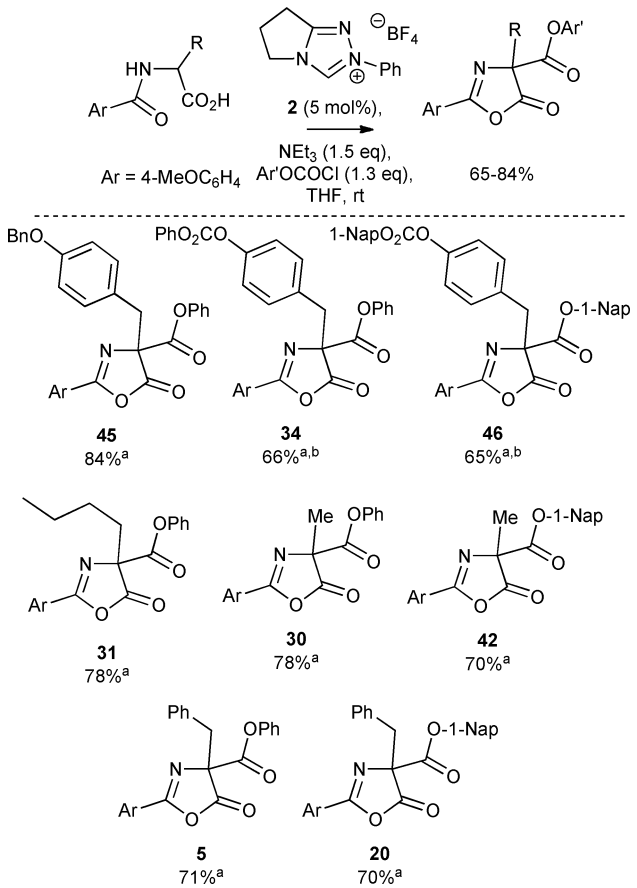

**Scheme 4** Two-step tandem reaction protocol [a]Isolated yield of homogeneous product after chromatographic purification.




**Scheme 5** DCC promoted cyclisation and domino reaction protocol [a]Isolated yield of homogeneous product after chromatographic purification.

participate in oxazolyl carbonate formation was attempted.[35] An excess of chloroformate was necessary in order to sequester the phenolate or naphtholate generated upon azlactone formation in this reaction cycle, generating the corresponding diaryl carbonate as a by-product.[36] In practice, addition of either phenyl or 1-naphthyl chloroformate (3 eq) to a solution of a range of *N*-acyl amino acids, $NEt_3$ (3.5 eq) and triazolium salt **2** (5 mol%)

proceeded to give the corresponding *C*-carboxyazlactones in 66–78% isolated yields (Scheme 6).



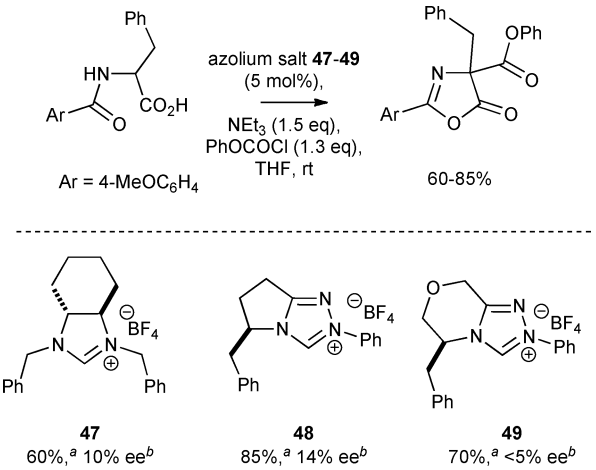

**Scheme 6** The development of domino multi-step reaction protocols [a]Isolated yield of homogeneous product after chromatographic purification. [b]Reaction conditions employed $NEt_3$ (5.5 eq), PhOCOCl (5 eq) or 1-NapOCOCl (5 eq), salt **2** (10 mol%), THF, rt.

### Domino asymmetric catalysis

After demonstrating the feasibility of this domino reaction process in the racemic series, the ability of chiral NHCs to promote an asymmetric version of this process was investigated. Screening of a range of chiral azolium salts **47–49** identified a number of NHCs that proved catalytically active in this process, but all gave disappointing levels of asymmetric induction (Scheme 7).

## Conclusion

In conclusion, the NHC generated from triazolium salt **2** with $NEt_3$ promotes the chemoselective rearrangement of aryl oxazolyl carbonates to their corresponding *C*-aryloxyazlactones. The mechanism of this transformation has been probed through a series of crossover experiments. The $NEt_3$ promoted NHC mediated rearrangement protocol can be incorporated into domino reaction sequences, although chiral NHCs only promote this reaction with low levels of enantioselectivity. Current investigations from this laboratory are focused upon developing alternative applications of NHCs in asymmetric catalysis.




**Scheme 7** Attempted asymmetric domino reaction protocol [a]Isolated yield of homogeneous product after chromatographic purification. [b]Determined by HPLC analysis.

## Experimental section

### General experimental

$^1$H NMR Spectra were recorded using a Bruker Avance 400 spectrometer and Bruker Avance 300 spectrometer at 400 MHz and 300 MHz respectively, using residual protonated solvent as a reference for internal lock. The chemical shift information ($\delta_H$) for each resonance signal are given in units of parts per million (ppm) relative to tetramethylsilane (TMS) where $\delta_H$ TMS = 0.00 ppm, or to residual (protonated) solvent. The number of protons (*n*) for a reported resonance signal are indicated by *n*H from their integral value and their multiplicity is reported with their coupling constants (*J*) quoted in Hz. Coupling constants are determined by analysis using iNMR® and Topspin®.

$^{13}$C NMR Spectra were recorded using a Bruker Avance 300 and Bruker Avance 400 spectrometer using the PENDANT sequence at 75.5 MHz and 100 MHz respectively with internal deuterated solvent lock. The chemical shift information ($\delta_C$) for each resonance signal is given in units of parts per million (ppm) relative to tetramethylsilane (TMS) where $\delta_C$ TMS = 0.00 ppm, or to the relevant solvent.

$^{19}$F NMR Spectra were recorded using a Bruker Avance 400 spectrometer at 282 MHz. The chemical shift information ($\delta_F$) for each resonance signal are given in units of parts per million (ppm) relative to trichlorofluoromethane ($CFCl_3$) where $\delta_F$ = 0.00.

Mass spectrometric (*m*/*z*) data were acquired by electrospray ionisation (ESI), electron impact (EI) or chemical ionisation (CI), either at the University of St Andrews Mass Spectrometry facility ([A] quoted) or at the EPSRC National Mass Spectrometry Service Centre, Swansea ($[A]^+$ or $[A]^-$ quoted). At the University of St Andrews, low and high resolution ESI MS was carried out on a Micromass LCT spectrometer and low and high resolution EI and CI MS was carried out on a Micromass GCT spectrometer. At the EPSRC National Mass Spectrometry Service Centre, low resolution ESI MS was carried out on a Waters Micromass ZQ4000 spectrometer and low resolution EI and CI MS was carried out on a Micromass Quattro II spectrometer. High resolution ESI and ESI MS was carried out on a Finnigan MAT 900 XLT or a Finnigan MAT 95 XP; a Thermofisher LTQ Orbitrap

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XL spectrometer was also used to obtain high resolution ESI MS for accurate mass determination but also provided fragmentation data for the characterisation of samples. Values are quoted as a ratio of mass to charge in Daltons.

Melting points were determined using an Electrothermal 9100 melting point apparatus and are uncorrected.

Optical rotations were determined using a PerkinElmer Model 341 Polarimeter, at 20.0 °C using a Na/Hal lamp tuned to 589 nm.

Chiral HPLC was performed on either a Varian ProStar or Gilson apparatus, using a CHIRALPAK OD-H, AD-H or AS-H silica column, 0.46 cm $\phi \times 25$ cm, using hexane and isopropanol as eluents.

Analytical thin layer chromatography (tlc) was carried out on pre-coated 0.20 mm Machery-Nagel Polygram SIL G/$UV_{254}$ silica plates. Visualisation was carried out by absorption of ultraviolet light or thermal decomposition after dipping in either an ethanolic solution of phosphomolybdic acid or an aqueous solution of potassium permanganate/sodium hydroxide.

Chromatography was performed using Merck Ltd. silica gel 40–63 μm, eluting with solvents supplied under a positive pressure of compressed air.

Anhydrous solvents were obtained from the MBraun SPS-800 solvent purification system.

Chemicals were purchased from Acros UK, Sigma-Aldrich UK, Alfa Aeasar UK, Fisher UK or Merck. Brine refers to a saturated aqueous solution of sodium chloride.

Reactions involving moisture sensitive reagents were performed under an atmosphere of $N_2$ or Ar using standard vacuum line techniques and with freshly distilled solvents. All glassware was flame-dried and allowed to cool under vacuum.

For known compounds, where certain elements of analytical data are not described in the literature, these data have been reported and are marked §.

### General procedures

**General procedure A (preparation of oxazolyl carbonates from azlactones).** Based upon a procedure by Fu and co-workers,[18a] $Et_3N$ (1.1–1.5 equiv) was added to a stirred solution of the desired azlactone (1 equiv) in THF at 0 °C, followed by addition of the desired chloroformate (1.06 equiv). The mixture was stirred at 0 °C for 30 min before warming to ambient temperature and stirring over 16 h. The resulting solution was poured into $H_2O$ and the aqueous phase extracted with $Et_2O$ (× 3). The organic extracts were combined, washed with 0.1 M HCl(aq), sat $NaHCO_3$(aq) solution, brine, dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by recrystallisation or silica chromatography ($Et_2O$/petrol) gave the desired product.

### Procedures for Steglich rearrangement

**General procedure B (standard protocol).** To a mixture of azolium salt ($x$ mol%) in solvent (typically THF, ~1 mL per 100 mg of carbonate) was added a solution of base in solvent (0.9$x$ mol%). The mixture was stirred for 20 min then a solution of carbonate (1 equiv) in solvent (typically THF, ~1 mL per 100 mg of carbonate) was added *via* cannula. The mixture was stirred for $y$ min (typically <60 min) then concentrated *in vacuo* and, if necessary, the residue was purified by silica chromatography.

**General procedure C (one-pot).** To a mixture of azolium salt ($x$ mol%) and carbonate (1 equiv) in THF or toluene (~1 mL per 100 mg of carbonate) was added a solution of base in solvent (0.9$x$ mol%). The mixture was stirred for $y$ min then concentrated *in vacuo* and, if necessary, the residue was purified by silica chromatography.

For crossover experiments, 0.5 equiv of both carbonate substrates were combined in the relevant solvent, and following the aforementioned general procedure B, a sample of the product mixture was concentrated *in vacuo* then examined spectroscopically to determine the product distributions.

**General procedure D (two-step domino cascade).** To a mixture of azlactone (1 equiv) and triazolium salt (5 mol%) in THF (~1 mL per 100 mg of azlactone) was added $Et_3N$ (1.5 equiv) followed by the requisite aryl chloroformate (1.3 equiv). The mixture was stirred at ambient temperature, then $Et_3N$·HCl was removed by filtration and the filtrate concentrated *in vacuo*. Purification by silica chromatography (EtOAc/petrol, $Et_2O$/petrol or $CH_2Cl_2$/petrol) gave the desired product.

**General procedure E (multi-step domino cascade with DCC).** A mixture of *N*-(*p*-anisoyl) amino acid (1 equiv) and DCC (1.01 equiv) were stirred in THF for 2 h then filtered (to remove dicyclohexylurea), followed by addition of triazolium salt **2** (5 mol%), $Et_3N$ (1.5 equiv) and then phenyl chloroformate (1.3 equiv). The mixture was stirred at ambient temperature, then $Et_3N$·HCl was removed by filtration and the filtrate concentrated *in vacuo*. Purification by silica chromatography ($Et_2O$/petrol) gave the desired product.

**General procedure F (multi-step domino cascade with aryl chloroformates).** To a mixture of *N*-(*p*-anisoyl) amino acid (1 equiv) and triazolium salt **2** (5–10 mol%) in THF was added $Et_3N$ (3.5 equiv) followed by phenyl chloroformate (3 equiv), with significant exotherm and effervescence observed. The mixture was stirred at ambient temperature for 5–60 min, then $Et_3N$·HCl was removed by filtration and the filtrate concentrated *in vacuo*. Purification by silica chromatography ($Et_2O$/petrol or $CH_2Cl_2$/petrol) gave the desired product.

**Known substrates and rearrangement products.** Known azlactone precursors, carbonate substrates and their *C*-carboxyazlactone isomers were prepared following literature procedures with physical and spectroscopic data in agreement with the literature (for **4** and **5** see ref. 18a; for **11**, **12**, **17**, **18**, **24**, **25**, **26**, **28**, **29**, **31**, **32**, **33**, **35**, **36**, **37**, **38**, **39** and **40** see ref. 19b; for **13** and **19** see ref. 16a; for **23** and **30** see ref. 18b. Spectroscopic data of purified materials were used to identify product distributions in crossover experiments.

Literature procedures were used for the preparation of compounds **2**,[19b] **6**,[19b] **7**,[19b] **9**,[19b] **10**,[19b] **47**[14a] and **48**,[37] giving analytical and spectroscopic data in accordance with the literature.

### (*R*)- and (*RS*)-Phenyl 4-benzyl-5-oxo-2-(4-methoxyphenyl)-4,5-dihydrooxazole-4-carboxylate 5

**Using catalytic base.** Following general procedure C, carbonate **4** (100 mg, 0.249 mmol), triazolium salt **2** (6.80 mg, 0.0249 mmol), THF (1 mL) and $Et_3N$ (3.12 μL, 0.0224 mmol)

gave, after 120 min and chromatography (10% EtOAc : petrol), ester (±)-**5** as a colourless oil (82.0 mg, 82%).

**Using stoichiometric base.** Following general procedure C, carbonate **4** (100 mg, 0.249 mmol), triazolium salt **2** (6.80 mg, 0.0249 mmol), THF (1 mL) and $Et_3N$ (34.7 μL, 0.249 mmol) gave, after 5 min and chromatography (10% EtOAc:petrol), ester (±)-**5** as a colourless oil (82.1 mg, 82%).

**Two-step domino cascade.** Following general procedure D, azlactone (200 mg, 0.711 mmol), triazolium salt **2** (9.70 mg, 0.0355 mmol), THF (2 mL), $Et_3N$ (128 μL, 0.924 mmol) and phenyl chloroformate (88.0 μL, 0.782 mmol) gave, after chromatography (10% EtOAc : petrol), ester (±)-**5** as a colourless oil (231 mg, 81%).

**Multi-step domino cascade with DCC.** Following general procedure E, *N*-*p*-anisoyl-DL-phenylalanine (300 mg, 1.00 mmol), DCC (208 mg, 1.01 mmol), triazolium salt **2** (13.7 mg, 0.0500 mmol), THF (3 mL), $Et_3N$ (182 μL, 1.30 mmol), and phenyl chloroformate (123 μL, 1.10 mmol) gave, after chromatography (20% $Et_2O$/petrol), ester (±)-**5** as a colourless oil (285 mg, 71%).

**Multi-step domino cascade with phenyl chloroformate.** Following general procedure F, *N*-*p*-anisoyl-DL-phenylalanine (300 mg, 1.00 mmol), $Et_3N$ (0.487 mL, 3.51 mmol), triazolium salt **2** (13.7 mg, 0.0500 mmol), THF (3 mL) and phenyl chloroformate (0.340 mL, 3.01 mmol) gave, after chromatography (20% $Et_2O$ : petrol), ester (±)-**5** as a colourless oil (286 mg, 71%).

$\delta_H$ (300 MHz, $CDCl_3$) 7.92–7.87 (2H, m, MeOAr*H*-2,6), 7.43–7.37 (2H, m, Ph*H*), 7.30–7.19 (6H, m, Ph*H*), 7.15–7.10 (2H, m, Ph*H*), 6.98–6.94 (2H, m, MeOAr*H*-2,6), 3.88 (3H, s, ArOC$H_3$), 3.75 (1H, ABd, *J* 13.7, C$H_A$H$_B$Ph) and 3.61 (1H, ABd, *J* 13.7, CH$_A$$H_B$Ph). Spectroscopic data are in accordance with the literature.[19b]

**Asymmetric multi-step domino cascades.** Following general procedure E, *N*-*p*-anisoyl-DL-phenylalanine (150 mg, 0.500 mmol), $Et_3N$ (0.243 mL, 1.75 mmol), chiral triazolium salt **47–49** (0.0250 mmol), THF (1.5 mL) and phenyl chloroformate (0.170 mL, 1.50 mmol) gave, after chromatography (20% $Et_2O$ : petrol), ester (*R*)-5 as a colourless oil:

Using triazolium salt **47**, 60% isolated yield, 10% *ee*.

Using triazolium salt **48**, 85% isolated yield, 14% *ee*.

Using triazolium salt **49**, 70% isolated yield, <5% *ee*.

Enantiomeric excesses were determined by HPLC with Chiralcel OD-H column (5% *i*-PrOH : hexane, flow rate = 1.0 mL min$^{-1}$), $t_R$(*R*) 13.8 min and $t_R$(*S*) 18.9 min.

### 4-Benzyl-2-(4-methoxyphenyl)oxazol-5-yl naphthalen-1-yl carbonate 14

Following general procedure A, $Et_3N$ (0.594 mL, 4.27 mmol), phenylalanine-derived azlactone (1.00 g, 3.56 mmol), $CH_2Cl_2$ (10 mL) and 1-naphthyl chloroformate (0.660 mL, 4.09 mmol), gave the crude product as a yellow oil. Crystallisation ($Et_2O$ : hexane) gave the product as a colourless solid (828 mg, 51%). mp 86–88 °C; $\delta_H$ (400 MHz, $CDCl_3$) 7.95–7.89 (4H, m, MeOAr*H*-3,5 and Nap*H*), 7.80 (1H, d, *J* 8.3, Nap*H*), 7.57 (2H, dt, 6.7, 3.0, Ar*H*), 7.49 (1H, t, *J* 8.0, Ar*H*), 7.39–7.31 (5H, m, Ar*H*), 7.27–7.24 (1H, m, Ar*H*), 6.95 (2H, d, *J* 8.8, MeOAr*H*-2,6), 3.97 (2H, s, PhC$H_2$) and 3.85 (3H, s, OC$H_3$); $\delta_C$ (100 MHz, $CDCl_3$) 161.7 (MeOAr*C*-1), 155.7 (Ar*C*), 150.2 (Ar*C*), 146.6 (Ar*C*), 145.9 (Ar*C*), 137.6 (Ar*C*), 134.8 (Ar*C*), 129.1 (Ar*C*H), 128.8 (Ar*C*H), 128.3 (Ar*C*H), 128.0 (Ar*C*H), 127.2 (Ar*C*H), 127.2 (Ar*C*H), 127.1 (Ar*C*H), 126.9 (Ar*C*H), 126.1 (Ar*C*), 125.4 (Ar*C*H), 123.5 (Ar*C*), 120.9 (Ar*C*H), 119.9 (Ar*C*), 117.3 (Ar*C*H), 114.4 (Ar*C*H), 55.6 (O*C*H$_3$) and 31.9 (*C*H$_2$); *m*/*z* MS (ESI+) 469 (100, [M + $NH_4$]$^+$), HRMS (ESI+) $C_{28}H_{25}N_2O_5^+$ ([M + $NH_4$]$^+$) requires 469.1758, found 469.1758 (+0.0 ppm); IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3052 (Ar C–H), 3027, 2970, 2913, 2835, 1792 (C═O), 1667 (Ar C═C), 1617 (C═N), 1603 (Ar C═C), 1459, 1502, 1455, 1434, 1393, 1307, 1258 (C–O), 1213 (C–O) and 1180 (C–O).

### Naphthalen-1-yl 4-benzyl-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate 20

Following general procedure C, carbonate **14** (100 mg, 0.221 mmol), triazolium salt **2** (6.05 mg, 0.0221 mmol), THF (1 mL) and $Et_3N$ (2.77 μL, 0.0199 mmol) gave, after 120 min and chromatography (10% EtOAc : petrol), ester (±)-**20** as a colourless oil (84.9 mg, 85%).

Following general procedure D, azlactone (200 mg, 0.711 mmol), triazolium salt **2** (9.70 mg, 0.0355 mmol), THF (2 mL), $Et_3N$ (128 μL, 0.924 mmol) and 1-naphthyl chloroformate (127 μL, 0.782 mmol) gave, after chromatography (10% EtOAc:petrol), ester (±)-**20** as a colourless oil (273 mg, 85%).

Following general procedure E, *N*-*p*-anisoyl-DL-phenylalanine (300 mg, 1.00 mmol), DCC (208 mg, 1.01 mmol), triazolium salt **2** (13.7 mg, 0.0500 mmol), THF (3 mL), $Et_3N$ (182 μL, 1.30 mmol), and 1-naphthyl chloroformate (0.179 mL, 1.10 mmol) gave, after chromatography (20% $Et_2O$ : petrol), ester (±)-**20** as a colourless oil (361 mg, 80%).

Following general procedure F, *N*-*p*-anisoyl-DL-phenylalanine (200 mg, 0.668 mmol), 1-naphthyl chloroformate (0.325 mL, 2.00 mmol), $Et_3N$ (0.325 mL, 2.34 mmol), triazolium salt **2** (9.12 mg, 33.4 μmol) and THF (2 mL), gave, after chromatographic purification (20% EtOAc : petrol), the product as a colourless oil (232 mg, 70%).

$\delta_H$ (400 MHz, $CDCl_3$) 7.96–7.90 (2H, m, MeOAr*H*-3,5), 7.88–7.83 (2H, m, Nap*H*), 7.76 (1H, br d, *J* 8.1, Ar*H*), 7.54–7.48 (2H, m, Ar*H*), 7.45 (1H, t, *J* 8.2, Ar*H*), 7.33–7.17 (6H, m, Ar*H*), 6.97–6.63 (2H, m, MeOAr*H*-2,6), 3.86 (3H, s, OC$H_3$), 3.81 (1H, ABd, *J* 13.7, PhC$H_A$H$_B$) and 3.68 (1H, ABd, *J* 13.7, PhCH$_A$$H_B$); $\delta_C$ (100 MHz, $CDCl_3$) 174.0 (*C*-2), 164.6 (MeOAr*C*-1), 163.7 (*C*OOAr), 163.5 (Ar*C*), 151.9 (Ar*C*), 146.0 (Ar*C*), 134.6 (Ar*C*), 132.8 (Ar*C*), 130.5 (Ar*C*H), 130.3 (Ar*C*H), 128.4 (Ar*C*H), 128.0 (Ar*C*H), 127.7 (Ar*C*H), 126.9 (Ar*C*H), 126.8 (Ar*C*H), 126.7 (Ar*C*H), 126.3 (Ar*C*H), 125.2 (Ar*C*H), 121.0 (Ar*C*H), 117.1 (Ar*C*), 114.3 (MeOAr*C*-2,6), 77.9 (*C*-4), 55.6 (O*C*H$_3$) and 40.1 (*C*H$_2$); *m*/*z* MS (ESI+) 451 (42, [M + H]$^+$), 407 (100, [M + MeOH – Ph]$^+$); HRMS (ESI+) $C_{23}H_{22}O_2N$ ([M + H]$^+$) requires 344.1645, found 344.1647 (+0.4 ppm); IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3063, 3033, 2965, 2937, 2841, 1822 (C═O), 1770 (C═O), 1645 (C═N), 1606 (Ar C═C), 1575, 1512, 1495 (Ar C═C), 1442, 1426, 1390, 1307, 1263 (C–O), 1212 (C–O) and 1173 (C–O).

### 4-Benzyl-2-(4-methoxyphenyl)oxazol-5-yl (4-methoxyphenyl) carbonate 15

Following general procedure A, $Et_3N$ (0.920 mL, 6.60 mmol), phenylalanine-derived azlactone (1.16 g, 4.12 mmol), THF

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(20 mL) and 4-methoxyphenyl chloroformate (1.84 mL, 12.4 mmol) gave the crude product as a yellow oil. Crystallisation ($Et_2O$ : petrol) gave the product as a colourless solid (1.44 g, 81%). mp 86–87 °C; $\delta_H$ (400 MHz, $CDCl_3$) 7.81–7.77 (2H, m, MeOAr*H*-3,5), 7.24–7.06 (4H, m, Ar*H*), 6.99–6.96 (2H, m, MeOAr*H*-2,6), 6.84–6.78 (5H, Ar*H*), 3.74 (2H, s, PhC$H_2$), 3.74 (3H, s, OC$H_3$) and 3.70 (3H, s, ArOC$H_3$). $\delta_C$ (100 MHz, $CDCl_3$) 161.6 (MeOAr*C*), 158.0 (MeOAr*C*), 155.6 (Ar*C*), 150.5 (Ar*C*), 147.5 (Ar*C*), 144.4 (Ar*C*), 137.6 (Ar*C*), 129.1 (Ar*C*H), 128.7 (Ar*C*H), 127.9 (Ar*C*H), 126.8 (Ar*C*), 123.4 (Ar*C*H), 121.5 (Ar*C*), 119.9 (Ar*C*), 114.7 (Ar*C*H), 114.3 (Ar*C*H), 55.8 (O*C*$H_3$), 55.6 (O*C*$H_3$) and 31.8 (*C*$H_2$); *m/z* MS (NSI+) 376 (100, $[M + H]^+$), HRMS (NSI+) $C_{22}H_{18}NO_5^+$ requires 375.3741, found 375.3737, (–1.1 ppm); IR $\nu_{max}$ (KBr)/$cm^{-1}$ 2961 (Ar C–H), 2837, 1785 (C═O), 1672 (Ar C═C), 1614 (C═N), 1601 (Ar C═C), 1498, 1460, 1254 (C–O), 1220 (C–O) and 1170 (C–O).

### 4-Methoxyphenyl 4-benzyl-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate 21

Following general procedure C, carbonate **15** (100 mg, 0.231 mmol), triazolium salt **2** (6.50 mg, 0.0231 mmol), THF (1 mL) and $Et_3N$ (32.2 µL, 0.231 mmol) gave, after 120 min and chromatography (10% $Et_2O$ : petrol), ester (±)-**21** as a colourless oil (40.1 mg, 40%). $\delta_H$ (300 MHz, $CDCl_3$) 7.89–7.86 (2H, m, MeOAr*H*-3,5), 7.27–7.19 (5H, m, Ph*H*), 7.04–7.01 (2H, m, MeOAr*H*), 6.95–6.93 (2H, m, MeOAr*H*), 6.88–6.86, (2H, m, MeOAr*H*), 3.86 (3H, s, ArOC$H_3$), 3.79 (3H, s, OC$H_3$), 3.72 (1H, ABd, *J* 13.7, PhC$H_A$H$_B$) and 3.59 (1H, ABd, *J* 13.7, PhCH$_A$$H_B$); $\delta_C$ (100 MHz, $CDCl_3$) 174.1 (MeOAr*C*), 165.3 (MeOAr*C*), 164.1 (Ar*C*), 163.5 (Ar*C*), 158.1 (Ar*C*), 144.2 (Ar*C*), 133.3 (Ar*C*), 130.9 (Ar*C*H), 130.6 (Ar*C*H), 128.7 (Ar*C*H), 128.1 (Ar*C*), 122.4 (Ar*C*H), 122.2 (Ar*C*), 117.7 (Ar*C*), 114.9 (Ar*C*H), 114.7 (Ar*C*H), 56.0 (O*C*$H_3$), 55.9 (O*C*$H_3$) and 40.7 (*C*$H_2$); *m/z* MS (NSI+) 432 (100, $[M + H]^+$), HRMS (NSI+) $C_{25}H_{22}NO_6^+$ requires 432.1442, found 432.1440, (–0.4 ppm); IR $\nu_{max}$ (thin film)/$cm^{-1}$ 2965 (Ar C–H), 2840, 1785 (C═O), 1670 (Ar C═C), 1614 (C═N), 1508 (Ar C═C), 1494, 1459, 1225 (C–O), 1217 (C–O) and 1170 (C–O).

### 4-Benzyl-2-(4-methoxyphenyl)oxazol-5-yl (4-fluorophenyl) carbonate 16

Following general procedure A, $Et_3N$ (0.920 mL, 6.60 mmol), phenylalanine-derived azlactone (1.16 g, 4.12 mmol), THF (20 mL) and 4-fluorophenyl chloroformate (1.62 mL, 12.4 mmol) gave the crude product as a yellow oil. Crystallisation ($Et_2O$ : petrol) gave the product as a colourless solid (1.56 g, 90%). mp 81–83 °C; $\delta_H$ (300 MHz, $CDCl_3$) 7.82–7.77 (2H, m, MeOAr*H*-3,5), 7.22–7.14 (5H, m, Ar*H*), 7.06–6.94 (4H, Ar*H*), 6.85–6.80 (2H, m, MeOAr*H*-2,6), 3.82 (2H, s, C$H_2$Ph) and 3.73 (3H, s, OC$H_3$); $\delta_C$ (75 MHz, $CDCl_3$) 161.5 (MeOAr*C*), 160.7 (d, *J* 246.0, *p*FAr*C*), 155.5 (Ar*C*), 150.1 (Ar*C*), 146.5 (d, *J* 2.8, *p*FAr*C*), 145.6 (Ar*C*), 137.4 (Ar*C*), 129.0 (Ar*C*H), 128.6 (Ar*C*H), 127.8 (Ar*C*H), 126.7 (Ar*C*), 123.4 (Ar*C*H), 122.1 (d, *J* 8.7, *p*FAr*C*), 119.8 (Ar*C*), 116.4 (d, *J* 23.8, *p*FAr*C*), 114.2 (Ar*C*H), 55.4 (O*C*$H_3$), and 31.8 (*C*$H_2$); $\delta_F$ (282 MHz, $CDCl_3$) 115.6; *m/z* MS (NSI+) 420 (100, $[M + H]^+$), HRMS (NSI+) $C_{24}H_{19}FNO_5^+$ requires 420.1242, found 420.1242, (–0.9 ppm); IR $\nu_{max}$ (KBr)/$cm^{-1}$ 3075, 2944 (Ar C–H), 2839, 1787 (C═O), 1670 (Ar C═C), 1615 (C═N), 1589 (Ar C═C), 1503, 1454, 1261 (C–O), 1218 (C–O), 1187 (C–O) and 1167.

### 4-Fluorophenyl 4-benzyl-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate 22

Following general procedure C, carbonate **16** (100 mg, 0.231 mmol), triazolium salt **2** (6.5 mg, 0.0238 mmol), THF (1 mL) and $Et_3N$ (33.2 µl, 0.238 mmol gave, after 120 min and chromatography (20% $Et_2O$ : petrol) ester (±)-**22** as a colourless oil (31.4 mg, 31%). $\delta_H$ (300 MHz, $CDCl_3$) 7.91–7.89 (2H, m, MeOAr*H*-3,5), 7.29–7.21 (5H, m, Ph*H*), 7.11–7.08 (4H, m, *p*FAr*H*), 6.97–6.95, (2H, m, MeOAr*H*-2,6), 3.88 (3H, s, OC$H_3$), 3.73 (1H, ABd, *J* 13.7, PhC$H_A$H$_B$) and 3.61 (1H, ABd, *J* 13.7, PhCH$_A$$H_B$); $\delta_C$ (100 MHz, $CDCl_3$) 173.7 (MeOAr*C*), 164.8 (Ar*C*), 163.8 (Ar*C*), 163.3 (ArC), 160.7 (d, *J* 245.4, *p*FAr*C*), 146.1 (d, *J* 2.7, *p*FAr*C*), 132.8 (Ar*C*), 130.6 (Ar*C*H), 130.3 (Ar*C*H), 128.5 (Ar*C*H), 127.8 (Ar*C*H), 122.8 (d, *J* 8.6, *p*FAr*C*), 117.2 (Ar*C*), 116.4 (d, *J* 23.7, *p*FAr*C*), 114.4 (Ar*C*H), 77.6 (Ar*C*), 55.7 (O*C*$H_3$) and 40.4 (*C*$H_2$); $\delta_F$ (282 MHz, $CDCl_3$) 116.2; *m/z* MS (NSI+) 452 (100, $[M + H + CH_3OH]^+$), HRMS (NSI+) $C_{25}H_{23}FNO_6^+$ requires 452.1504 found 452.1498, (–1.3 ppm); IR $\nu_{max}$ (thin film)/$cm^{-1}$ 2966 (Ar C–H), 2842, 1823, 1770 (C═O), 1645 (Ar C═C), 1607 (C═N), 1504 (Ar C═C), 1456, 1456, 1262 (C–O) and 1178 (C–O).

### (*RS*)-Phenyl methyl-5-oxo-2-(4-methoxyphenyl)-4,5-dihydro-oxazole-4-carboxylate 30

Following general procedure C, carbonate **23** (100 mg, 0.307 mmol), triazolium salt **2** (8.39 mg, 0.0307 mmol), THF (1 mL) and $Et_3N$ (3.85 µL, 0.0276 mmol) gave, after 120 min and chromatography (10% EtOAc : petrol), ester (±)-**30** as a colourless oil (81.0 mg, 81%).

Following general procedure D, alanine-derived azlactone (300 mg, 1.46 mmol), triazolium salt **2** (39.9 mg, 0.146 mmol), THF (3 mL), $Et_3N$ (305 µL, 2.19 mmol) and phenyl chloroformate (214 µL, 1.90 mmol) gave, after chromatography (10% EtOAc : petrol), ester (±)-**30** as a colourless oil (385 mg, 81%).

Following general procedure E, *N*-*p*-anisoyl-DL-alanine (200 mg, 0.896 mmol), DCC (187 mg, 0.905 mmol), triazolium salt **2** (12.2 mg, 0.0448 mmol), THF (2 mL), $Et_3N$ (186 µL, 1.34 mmol), and phenyl chloroformate (132 µL, 1.17 mmol) gave, after chromatography (20% $Et_2O$ : petrol), ester (±)-**30** as a colourless oil (201 mg, 69%).

Following general procedure F, *N*-*p*-anisoyl-DL-alanine (500 mg, 2.24 mmol), $Et_3N$ (1.09 mL, 7.84 mmol), triazolium salt **2** (30.5 mg, 0.112 mmol), THF (4 mL) and phenyl chloroformate (760 µL, 6.72 mmol) gave, after chromatography (20% $Et_2O$ : petrol), ester (±)-**30** as a colourless oil (568 mg, 78%).

$\delta_H$ (300 MHz, $CDCl_3$) 7.97–7.92 (2H, m, MeOAr*H*-3,5), 7.34–7.25 (2H, m, Ph*H*-2,6), 7.19–7.13 (1H, m, Ph*H*-4), 7.05–6.99 (2H, m, Ph*H*-3,5), 6.95–6.90 (2H, m, MeOAr*H*-2,6), 3.81 (3H, s, OC$H_3$) and 1.80 (3H, s, C$H_3$). Spectroscopic data are in accordance with the literature.[19b]

### Phenyl 4-butyl-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate 31

Following general procedure C, carbonate **24** (100 mg, 0.272 mmol), triazolium salt **2** (7.43 mg, 0.0272 mmol), THF

(1 mL) and $Et_3N$ (3.41 μL, 0.0245 mmol) gave, after 120 min and chromatography (10% $Et_2O$ : petrol), ester (±)-**31** as a colourless oil (81.0 mg, 81%).

Following general procedure E, *N*-*p*-anisoyl-DL-norleucine (300 mg, 1.13 mmol), DCC (236 mg, 1.14 mmol), triazolium salt **2** (15.5 mg, 0.0568 mmol), THF (3 mL), $Et_3N$ (236 μL, 1.70 mmol), and phenyl chloroformate (166 μL, 1.47 mmol) gave, after chromatography (10% $Et_2O$ : petrol), ester (±)-**31** as a colourless oil (303 mg, 73%).

Following general procedure F, *N*-*p*-anisoyl-DL-norleucine (900 mg, 3.39 mmol), $Et_3N$ (1.65 mL, 11.9 mmol), triazolium salt **2** (46.3 mg, 0.170 mmol), THF (9 mL) and phenyl chloroformate (1.14 mL, 10.2 mmol) gave, after chromatographic purification (3% → 20% $Et_2O$ : petrol), ester (±)-**31** as a colourless oil (934 mg, 75%).

$\delta_H$ (400 MHz, $CDCl_3$) 8.06–8.02 (2H, m, MeOAr*H*-3,5), 7.69–7.34 (2H, m, Ph*H*-3,5), 7.26–7.22 (1H, m, Ph*H*-4), 7.13–7.10 (2H, m, Ph*H*-2,6), 7.03–6.99 (2H, m, MeOAr*H*-2,6), 3.88 (3H, s, $OCH_3$), 2.45–2.38 (1H, m, C(4)$H_AH_B$), 2.34–2.28 (1H, m, C(4)$H_AH_B$), 1.44–1.35 (3H, m, $CH_3CH_2CH_AH_B$), 1.31–1.21 (1H, m, $CH_3CH_2CH_AH_B$) and 0.91 (3H, t, *J* 7.1, $CH_3$); $\delta_C$ (100 MHz, $CDCl_3$) 174.5 (*C*OOCR$_2$), 164.8 (*C*OOPh), 163.9 and 163.3 (MeOAr*C*-1 and *C*═N), 150.4 (OPh*C*-1), 130.5 (MeOAr*C*H-3,5), 129.6 (OPh*C*H-3,5), 126.6 (OPh*C*H-4), 121.2 (OPh*C*H-2,6), 117.4 (MeOAr*C*-4), 114.5 (MeOAr*C*H-2,6), 76.8 (*C*-4), 55.7 ($OCH_3$), 34.3 ($CH_2$), 25.5 ($CH_2$), 22.6 ($CH_2CH_3$) and 13.9 ($CH_3$); *m*/*z* MS (ESI+) 386 (100, [M + H]), 248 (72, [M – COOPh + H]) and 135 (38, ArC≡O); HRMS (ESI+) $C_{21}H_{22}NO_5$ ([M + H]) requires 368.1489, found 368.1498 (–2.4 ppm); IR $\nu_{max}$ (thin film)/cm$^{-1}$ 2961, 2934, 2874, 1823 (C═O), 1771 (C═O), 1653 (C═N), 1609, 1513, 1308, 1262 (C–O) and 1173 (C–O).

### Phenyl isobutyl-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate 32

Following general procedure C, carbonate **25** (100 mg, 0.272 mmol), triazolium salt **2** (7.43 mg, 0.0272 mmol), THF (1 mL) and $Et_3N$ (3.41 μL, 0.0245 mmol) gave, after 120 min and chromatography (10% $Et_2O$ : petrol), ester (±)-**32** as a colourless oil (77.8 mg, 78%).

Following general procedure D, leucine-derived azlactone (200 mg, 0.809 mmol), triazolium salt **9** (11.1 mg, 0.0405 mmol), THF (2 mL), $Et_3N$ (157 μL, 1.13 mmol) and phenyl chloroformate (119 μL, 1.05 mmol) gave, after chromatography (15% $Et_2O$ : petrol), ester (±)-**32** as a colourless oil (252 mg, 85%).

Following general procedure E, *N*-*p*-anisoyl-DL-leucine (300 mg, 1.13 mmol), DCC (236 mg, 1.14 mmol), triazolium salt **2** (15.1 mg, 0.0552 mmol), THF (3 mL), $Et_3N$ (236 μL, 1.70 mmol) and phenyl chloroformate (166 μL, 1.47 mmol) gave, after chromatography (15% $Et_2O$ : petrol), ester (±)-**32** as a colourless oil (290 mg, 70%).

$\delta_H$ (400 MHz, $CDCl_3$) 8.07–8.04 (2H, m, MeOAr*H*-3,5), 7.45–7.09 (5H, m, Ph*H*), 7.05–6.99 (2H, m, MeOAr*H*-2,6), 3.90 (3H, s, $OCH_3$), 2.48 (1H, ABX, $J_{AB}$ 14.1, $J_{AX}$ 6.0, $CH_AH_BCH(CH_3)_2$), 2.17 (1H, ABX, $J_{BA}$ 14.1, $J_{BX}$ 7.2, $CH_AH_BCH(CH_3)_2$), 1.83 (1H, app sept, *J* 6.6, $CH(CH_3)_2$), 1.01 (3H, d, *J* 6.6, $CH(CH_3)_2$) and 0.97 (3H, d, *J* 6.6, $CH(CH_3)_2$). Spectroscopic data are in accordance with the literature.[19b]

### Phenyl 2-(4-methoxyphenyl)-5-oxo-4-phenyl-4,5-dihydrooxazole-4-carboxylate 33

Following general procedure C, carbonate **26** (100 mg, 0.258 mmol), triazolium salt **2** (7.04 mg, 0.0258 mmol), THF (1 mL) and $Et_3N$ (3.24 μL, 0.0232 mmol) gave, after 120 min and chromatography (15% $Et_2O$ : petrol), ester (±)-**33** as a colourless oil (72.2 mg, 72%).

Following general procedure D, phenylglycine-derived azlactone (200 mg, 0.748 mmol), triazolium salt **9** (10 mg, 0.0374 mmol), THF (2 mL), $Et_3N$ (135 μL, 0.972 mmol) and phenyl chloroformate (93.0 μL, 0.823 mmol) gave, after chromatography (20% $Et_2O$ : petrol), ester (±)-**33** as a colourless oil (217 mg, 75%).

$\delta_H$ (400 MHz, $CDCl_3$) 8.15–8.12 (2H, m, MeOAr*H*-3,5), 7.86–7.84 (2H, m, Ph*H*), 7.49–7.42 (3H, m, Ph*H*), 7.38–7.33 (2H, m, Ph*H*), 7.23 (1H, tt, *J* 7.4, 1.4, Ph*H*-4), 7.11–7.09 (2H, m, Ph*H*-2,6), 7.05–7.02 (2H, m, MeOAr*H*-2,6) and 3.90 (3H, s, $OCH_3$). Spectroscopic data are in accordance with the literature.[19b]

### Phenyl 2-(4-methoxyphenyl)-5-oxo-4-(4-phenoxycarbonyloxy)-benzyl-4,5-dihydrooxazole-4-carboxylate 34

Following general procedure C, carbonate **27** (100 mg, 0.186 mmol), triazolium salt **2** (5.08 mg, 0.0186 mmol), THF (1 mL) and $Et_3N$ (2.33 μL, 0.0167 mmol) gave, after 120 min and chromatography (10% $Et_2O$ : petrol), ester (±)-**34** as a colourless oil (77.0 mg, 77%).

Following a stoichiometric modification to general procedure F, *N*-*p*-anisoyl-DL-tyrosine (250 mg, 0.793 mmol), $Et_3N$ (661 μL, 4.76 mmol), triazolium salt **2** (10.8 mg, 0.0397 mmol), THF (2.5 mL) and phenyl chloroformate (493 μL, 4.36 mmol) gave, after chromatographic purification (20% $Et_2O$ : petrol), ester (±)-**34** as a colourless oil (281 mg, 66%).

$\delta_H$ (300 MHz, $CDCl_3$) 7.91–7.86 (2H, m, MeOAr*H*-3,5), 7.43–7.32 (5H, m, Ar*H*), 7.32–7.27 (2H, m, Ar*H*), 7.26–7.22 (3H, m, Ar*H*), 7.21–7.08 (4H, m, Ar*H*), 6.97–6.92 (2H, m, MeOAr*H*-2,6), 3.86 (3H, s, $OCH_3$), 3.74 (1H, ABd, *J* 13.8, $ArCH_AH_B$) and 3.59 (1H, ABd, *J* 13.8, $ArCH_aH_B$); $\delta_C$ (75 MHz, $CDCl_3$) 173.8 (*C*OOCR$_2$), 164.6 (*C*OOPh), 164.0 and 163.6 (MeOAr*C*-1 and *C*═N), 152.0 (Ar*C*), 151.2 (Ar*C*), 150.7 (Ar*C*), 150.5 (Ar*C*), 132.0 (Ar*C*H), 131.3 (Ar*C*H), 130.5 (Ar*C*H), 129.8 (Ar*C*H), 126.8 (Ar*C*H), 126.6 (MeOAr*C*-4), 121.4 (Ar*C*H), 121.2 (Ar*C*H), 121.1 (Ar*C*H), 121.0 (Ar*C*H), 117.2 (PhOC(O)OAr*C*-4), 114.6 (OAr*C*H-2,6), 77.6 (*C*-3), 55.8 ($OCH_3$) and 39.7 ($CH_2$); *m*/*z* MS (ESI+) 538 (100, $[M + H]^+$); HRMS (ESI+) $C_{31}H_{24}NO_8$ ([M + H]) requires 538.1501, found 538.1502 (–0.2 ppm); IR $\nu_{max}$ (thin film)/cm$^{-1}$ 2934 (CH), 2824 (CH), 2360 (CH), 1823 (C═O), 1773 (C═O), 1771 (C═O), 1646 (C═N), 1608, 1513, 1493, 1259, 1236 (C–O), 1185, 1161, 980, 841, 742 and 687.

### 2-(4-Methoxyphenyl)-4-methyloxazol-5-yl naphthalen-1-yl carbonate 41

Following general procedure A, $Et_3N$ (0.81 mL, 5.84 mmol), alanine derived azlactone (1.00 g, 5.84 mmol), THF (15 mL) and 1-naphthyl chloroformate (0.94 mL, 5.60 mmol) gave the crude product as a yellow oil. Crystallisation ($Et_2O$ : petrol) gave the product as a colourless solid (1.21 g, 66%). mp 120–122 °C; $\delta_H$ (400 MHz, $CDCl_3$) 8.07–8.04 (1H, m, Ar*H*), 7.94–7.91 (3H, m, Ar*H*), 7.84–7.80 (1H, m, Ar*H*), 7.64–7.55 (2H, m, Ar*H*),

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7.51–7.50 (2H, m, Ar*H*), 6.97–6.94 (2H, m, MeOAr*H*-2,6), 3.85 (3H, s, OC$H_3$) and 2.23 (3H, s, C$H_3$); $\delta_C$ (100 MHz, $CDCl_3$) 161.5 (MeOAr*C*), 155.3 (Ar*C*), 150.3 (Ar*C*), 146.6 (Ar*C*), 145.6 (Ar*C*), 134.8 (Ar*C*), 128.3 (Ar*C*H), 127.7 (Ar*C*H), 127.2 (Ar*C*H), 127.1 (Ar*C*H), 127.0 (Ar*C*H), 126.1 (Ar*C*), 125.4 (Ar*C*H), 120.6 (Ar*C*H), 120.4 (Ar*C*), 119.9 (Ar*C*), 117.3 (Ar*C*), 114.3 (Ar*C*H), 55.5 (O$CH_3$) and 10.6 ($CH_3$); *m/z* MS (NSI+) 432 (100, $[M + H]^+$), HRMS (NSI+) $C_{25}H_{22}NO_6^+$ requires 432.1442, found 432.1434, (–1.8 ppm); IR $\nu_{max}$ (KBr)/$cm^{-1}$ 1784 (C═O), 1670 (Ar C═C), 1615 (C═N), 1498, 1467, 1396, 1255 (C–O), 1224 (C–O) and 1173 (C–O).

### Naphthalen-1-yl 2-(4-methoxyphenyl)-4-methyl-5-oxo-4,5-dihydrooxazole-4-carboxylate 42

Following general procedure F, *N*-*p*-anisoyl-DL-alanine (200 mg, 0.896 mmol), $Et_3N$ (0.436 mL, 3.14 mmol), 1-naphthyl chloroformate (0.436 mL, 2.69 mmol), triazolium salt **2** (12.2 mg, 44.8 μmol) and THF (2 mL) gave, after chromatographic purification (20% $Et_2O$ : petrol), ester (±)-**42** as a colourless oil (235 mg, 70%). $\delta_H$ (400 MHz, $CDCl_3$) 8.10–8.06 (2H, m, MeOAr*H*-3,5), 7.88–7.83 (2H, m, Nap*H*-5,8), 7.75 (1H, br d, *J* 8.3, Nap*H*-4), 7.52–7.48 (2H, m, Nap*H*-6,7), 7.44 (1H, t, *J* 7.9, Nap*H*-3), 7.28 (1H, dd, *J* 7.6, 1.0, Nap*H*-2), 7.04–7.01 (2H, m, MeOAr*H*-2,6), 3.90 (3H, s, OC$H_3$) and 1.95 (3H, s, C$H_3$); $\delta_C$ (100 MHz, $CDCl_3$) 175.5 (*C*OOCR$_2$), 165.0 (*C*OOAr), 164.0 and 163.8 (MeOAr*C*-1 and *C*═N), 146.1 (Nap*C*-1), 134.7 (Nap*C*-4a), 130.5 (MeOAr*C*H-3,5), 128.1 (Nap*C*H-5), 127.0 (Nap*C*H), 126.9 (Nap*C*H), 126.8 (Nap*C*H), 126.4 (Nap*C*-8a), 125.3 (Nap*C*H-3), 121.0 (Nap*C*H-8), 117.9 (Nap*C*H-2), 117.5 (MeOAr*C*-4), 114.6 (MeOAr*C*H-2,6), 73.2 (Me*C*(COOAr)), 55.7 (O$CH_3$) and 20.6 ($CH_3$); *m/z* MS (ESI+) 408 (100, $[M + MeOH - H]^+$); HRMS (ESI+) $C_{23}H_{22}NO_6^+$ ($[M + MeOH + H]^+$) requires 408.1442, found 408.1440 (–0.5 ppm); IR $\nu_{max}$ (thin film)/$cm^{-1}$ 3057, 3009, 2937, 2842, 1826 (C═O), 1772 (C═O), 1645 (C═N), 1608, 1308, 1262 (C–O) and 1221 (C–O).

### Phenyl 4-(4-benzyloxyphenyl)-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate 45

Following general procedure E, *N*-*p*-anisoyl-DL-(*O*-benzyl)-tyrosine (200 mg, 0.493 mmol), DCC (103 mg, 0.498 mmol), triazolium salt **2** (7.04 mg, 0.0258 mmol), THF (2 mL), $Et_3N$ (104 μL, 0.747 mmol), and phenyl chloroformate (72.0 μL, 0.641 mmol) gave, after chromatography (20% $Et_2O$ : petrol), ester (±)-**45** as a colourless oil (210 mg, 84%).

Following general procedure F, *N*-*p*-anisoyl-DL-(*O*-benzyl)-tyrosine (200 mg, 0.493 mmol), $Et_3N$ (0.241 mL, 1.73 mmol), triazolium salt **2** (6.73 mg, 0.0247 mmol), THF (2 mL) and phenyl chloroformate (0.165 mL, 1.48 mmol) gave, after chromatography (10% $Et_2O$ : petrol), ester (±)-**45** as a colourless oil (210 mg, 84%).

$\delta_H$ (300 MHz, $CDCl_3$) 7.84–7.78 (2H, m, MeOAr*H*-3,5), 7.33–7.21 (7H, m, Ar*H*), 7.20–7.14 (1H, m, Ar*H*), 7.14–7.07 (2H, m, Ar*H*), 7.04–7.00 (2H, m, Ar*H*), 6.89–6.84 (2H, m, MeOAr*H*-2,6), 6.77–6.71 (2H, m, BnOAr*H*-2,6), 4.89 (2H, s, PhC$H_2$), 3.78 (3H, s, OC$H_3$), 3.59 (1H, ABd, *J* 13.8, BnOArC$H_AH_B$) and 3.47 (1H, ABd, *J* 13.8, BnOArC$H_AH_B$); $\delta_C$ (100 MHz, $CDCl_3$) 173.8 (*C*OOCR$_2$), 164.7 (*C*OOPh), 163.8 and 163.3 (MeOAr*C*-1 and *C*═N), 158.4 (BnOAr*C*-1), 150.4 (OPh*C*-1), 137.0 (CH$_2$Ph*C*-1), 131.8 (Ar*C*H), 130.4 (Ar*C*H), 129.7 (Ar*C*H), 128.7 (Ar*C*H), 128.1 (Ar*C*H), 127.6 (Ar*C*H), 126.7 (Ar*C*H), 125.2 (MeOAr*C*-4), 121.3 (Ar*C*H), 117.4 (BnOAr*C*-4), 114.8 (OAr*C*H-2,6), 114.5 (OAr*C*H-2,6), 77.8 (*C*-3), 70.0 (O$CH_2$), 55.7 (O$CH_3$) and 39.7 (BnOAr–$CH_2$); *m/z* MS (ESI+) 508 (10, $[M + H]^+$), 135 (38, ArC≡$O^+$) and 95 (100); HRMS (ESI+) $C_{31}H_{26}NO_6$ ($[M + H]^+$) requires 508.1763, found 508.1760 (+0.6 ppm); IR $\nu_{max}$ (thin film)/$cm^{-1}$ 3064 (CH), 3035 (CH), 2935 (CH), 2841 (CH), 1823 (C═O), 1766 (C═O), 1647, 1609, 1512, 1493, 1325, 1307 and 1262 (C–O).

### Naphthalen-1-yl 2-(4-methoxyphenyl)-4-(4-((naphthalen-1-yloxy)-carbonyloxy)benzyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate 46

Following a stoichiometric modification to general procedure F, *N*-*p*-anisoyl-DL-tyrosine (284 mg, 0.900 mmol), 1-naphthyl chloroformate (0.730 mL, 4.50 mmol), $Et_3N$ (0.690 mL, 4.95 mmol), triazolium salt 2 (12.3 mg, 0.045 mmol) and THF (4 mL), gave, after chromatographic purification (20% EtOAc : petrol), the ester (±)-**46** as a colourless oil (373 mg, 65%). $\delta_H$ (300 MHz, $CDCl_3$) 8.09–8.06 (1H, m, Ar*H*), 7.94–7.88 (2H, m, MeOAr*H*-3,5), 7.83–7.78 (2H, m, Ar*H*), 7.63–7.41 (10H, m, Ar*H*) 7.34–7.26 (3H, m, Ar*H*), 7.00–6.95 (2H, m, MeOAr*H*-2,6), 3.88 (1H, ABd, *J* 13.8, ArC$H_AH_B$), 3.87 (3H, s, OC$H_3$) and 3.74 (1H, ABd, *J* 13.7, ArC$H_AH_B$); $\delta_C$ (75 MHz, $CDCl_3$) 174.0 (*C*OOCR$_2$), 164.6 (MeOAr*C*-1), 163.9 (*C*OOAr), 163.8 (Ar*C*), 151.9 (Ar*C*), 150.7 (Ar*C*), 146.8, (Ar*C*), 134.7 (Ar*C*), 131.9 (Ar*C*H), 131.2 (Ar*C*), 130.4 (Ar*C*H), 128.14 (Ar*C*H), 128.07 (Ar*C*H), 127.1 (Ar*C*H), 126.9 (Ar*C*H), 126.8 (Ar*C*H), 126.6 (Ar*C*H), 126.5 (Ar*C*H), 126.5 (Ar*C*), 126.4 (Ar*C*), 125.4 (Ar*C*H), 125.3 (Ar*C*H), 121.0 (Ar*C*H), 120.9 (Ar*C*H), 117.9 (Ar*C*H), 117.5 (Ar*C*), 117.1 (Ar*C*), 114.5 (MeOAr*C*-2,6), 77.7 (*C*–N), 55.6 (O$CH_3$) and 39.4 (Ar–$CH_2$); *m/z* MS (CI+) 638.2 (100, $[M + H]^+$); HRMS (ESI+) $C_{39}H_{28}O_8N^+$ ($[M + H]^+$) requires 638.1809, found 638.1807 (–0.4 ppm); IR $\nu_{max}$ (KBr)/$cm^{-1}$ 3058, 3011, 2937, 2841, 1822 (C═O), 1776 (C═O), 1742 (C═O), 1654 (C═N), 1605 (Ar C═C), 1574, 1508, 1495 (Ar C═C), 1442, 1391, 1302, 1263 (C–O), 1229 (C–O), 1202 (C–O) and 1154 (C–O).

### (*S*)-5-Benzyl-2-phenyl-6,8-dihydro-5*H*-[1,2,4]triazolo[3,4-*c*][1,4]oxazin-2-ium tetrafluoroborate 49

To a mixture of sodium borohydride (2.60 g, 68.8 mmol) in THF (80 mL) was added L-phenylalanine (5.00 g, 30.2 mmol). The mixture was cooled to 0 °C and a solution of iodine (7.67 g, 30.2 mmol) in THF (20 mL) was added dropwise over 40 min. After gas evolution had ceased, the reaction was heated at reflux (80 °C) for 18 h. When the reaction had cooled to ambient temperature, MeOH was added slowly until the solution became clear and the mixture was stirred for a further 30 min. The mixture was concentrated *in vacuo* to afford a colourless paste, which was redissolved in KOH(aq) (20% w/v, 100 mL) with stirring over 4 h. The mixture was extracted with $CH_2Cl_2$ (150 mL × 2), the organics layers were combined, dried ($Na_2SO_4$), filtered and concentrated *in vacuo* to afford the crude product as a colourless solid. Recrystallisation from $Et_2O$ gave the product (*S*)-phenylalaninol as a colourless solid (2.49 g, 55%). mp 88–90 °C, lit.[38] 86–88 °C; $[\alpha]_D^{20}$ –22.3 (*c* 1.01, $CHCl_3$), lit.[38] –21.7 (*c* 1.0, $CHCl_3$); $\delta_H$ (400 MHz, $CDCl_3$) 7.36–7.18 (5H, m, Ph*H*), 3.66

(1H, ABX, $J_{AB}$ 10.6, $J_{AX}$ 3.9, C$H_A$H$_B$OH), 3.41 (1H, ABX, $J_{BA}$ 10.6, $J_{BX}$ 7.2, CH$_A$$H_B$OH), 3.18–3.11 (1H, m, C$H$NH$_2$), 2.82 (1H, ABX, $J_{AB}$ 13.5, $J_{AX}$ 5.2, PhC$H_A$H$_B$), 2.55 (1H, ABX, $J_{BA}$ 13.5, $J_{BX}$ 8.6, PhCH$_A$$H_B$) and 1.79 (2H, br s, N$H_2$). Data are in accordance with the literature.[38]

To a cooled (0 °C) solution of (*S*)-phenylalaninol (500 mg, 3.31 mmol) and $Et_3N$ (1.38 mL, 9.92 mmol) in $CH_2Cl_2$ (10 mL) was added chloroacetyl chloride (0.28 mL, 3.47 mmol) dropwise. The mixture was warmed to ambient temperature over 16 h then sat $NaHCO_3$(aq) (10 mL) added and the mixture extracted with $CH_2Cl_2$ (20 mL × 3). The organics were combined and washed with 1 M $H_2SO_4$(aq) (10 mL), $H_2O$ (10 mL) and brine (10 mL), then dried ($Na_2SO_4$), filtered and concentrated *in vacuo* to afford the crude amide intermediate as a brown oil which was used immediately in the subsequent step. The product was redissolved in THF (10 mL) and cooled to 0 °C before addition of potassium *tert*-butoxide (405 mg, 3.61 mmol). The mixture was warmed to ambient temperature over 90 min then concentrated *in vacuo* then partitioned between EtOAc (10 mL) and brine (10 mL). The aqueous fraction was extracted with EtOAc (10 mL × 2), then the combined organic fractions was dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford the crude morpholinone product. Chromatographic purification (40% EtOAc : petrol) gave the morpholinone as a colourless solid (420 mg, 66%). mp 85–87 °C, lit.[39] 86–87 °C; $[\alpha]_D^{20}$ +4.2 (*c* 1.0, MeOH), lit.[39] +4.0 (*c* 0.66 MeOH); $\delta_H$ (400 MHz, $CDCl_3$) 7.33–7.16 (5H, m, Ph$H$), 5.89 (1H, br s, N$H$), 4.22 (1H, ABq, *J* 17.8, OC$H_A$H$_B$CO), 4.19 (1H, ABq, *J* 17.8, OCH$_A$$H_B$CO), 3.88 (1H, ABX, $J_{AB}$ 11.5, $J_{AX}$ 3.8, OC$H_A$H$_B$CH), 3.77 (1H, ddd, *J* 9.2, 5.8, 3.8, NHC$H$), 3.46 (1H, ABX, $J_{BA}$ 11.5, $J_{BX}$ 5.8, OCH$_A$$H_B$CH), 2.85 (1H, ABX, $J_{AB}$ 13.5, $J_{AX}$ 5.8, C$H_A$H$_B$Ph) and 2.70 (1H, ABX, $J_{BA}$ 13.5, $J_{BX}$ 9.2, CH$_A$$H_B$Ph). Data are in accordance with the literature.[39] To a solution of lactam (400 mg, 2.09 mmol) in $CH_2Cl_2$ (12 mL) was added trimethyloxonium tetrafluoroborate (337 mg, 2.28 mmol) and the mixture was stirred for 16 h. To the mixture was then added phenylhydrazine (0.206 mL, 2.09 mmol) and the mixture was stirred for 20 h. The mixture was then concentrated *in vacuo* and redissolved in MeOH (1.5 mL) and triethyl orthoformate (4.5 mL). The mixture was heated at reflux (110 °C) for 16 h then cooled to ambient temperature, whereby the product had precipitated (in the event of no precipitation, the mixture was concentrated *in vacuo*, redissolved in EtOAc (5 mL), then $Et_2O$ (1 drop) was added to induce precipitation). The product was collected by filtration and washed with cold (–78 °C) EtOAc (~5 mL) to afford the triazolium salt **49** as a pale peach solid (230 mg, 29%). mp 190–195 °C; $[\alpha]_D^{20}$ –18.1 (*c* 0.8, MeOH); $\delta_H$ (400 MHz, $d_6$-DMSO) 10.91 (1H, s, NC$H$N), 7.90–7.88 (2H, m, Ph$H$), 7.76–7.71 (2H, m, Ph$H$), 7.71–7.65 (1H, m, Ph$H$-4), 7.43–7.40 (2H, m, NPh$H$-2), 7.36–7.32 (3H, m, NPh$H$), 5.23 (1H, ABq, *J* 16.2, OC$H_A$H$_B$), 5.15 (1H, ABq, *J* 16.2, OCH$_A$$H_B$), 4.85 (1H, app dq, *J* 9.7, 5.9, BnC$H$), 4.01–3.93 (2H, m, OC$H_2$CHBn), 3.50 (1H, ABX, $J_{AB}$ 13.6, $J_{AX}$ 5.9, PhC$H_A$H$_B$) and 3.18 (1H, ABX, $J_{BA}$ 13.6, $J_{BX}$ 9.7, PhCH$_A$$H_B$); $\delta_C$ (100 MHz, $d_6$-DMSO) 149.9 (N$C$HN), 135.1 (N=$C$), 134.9 (NAr$C$-1), 134.9 (CH$_2$Ph$C$-1), 130.8 (Ar$C$H-4), 130.4 (Ar$C$H), 129.5 (Ar$C$H), 129.0 (Ar$C$H), 127.5 (Ar$C$H), 120.7 (Ar$C$H), 65.1 (O$C$H$_2$), 61.5 (O$C$H$_2$), 56.3 (N$C$H) and 37.5 (Ph-$C$H$_2$); *m/z* MS (ESI+) 292 (100, $[M - BF_4]^+$); HRMS (ESI+) $C_{18}H_{18}ON_3^+$ ($[M - BF_4]^+$) requires 292.1444, found 292.1443 (–0.4 ppm); IR $\nu_{max}$ (KBr)/cm$^{-1}$ 3337, 3141, 3060 (Ar C–H), 3026, 2987, 2969, 1585 (C=N), 1536, 1497 (Ar C=C), 1469, 1118 (C–O) and 1054 (br).

## Acknowledgements

The authors would like to thank the Royal Society for a University Research Fellowship (ADS), The Carnegie Trust for the Universities of Scotland for a scholarship (CDC), The EPSRC (CJC), EaStCHEM and the University of St Andrews (JET) for funding, and the EPSRC National Mass Spectrometry Service Centre (Swansea).

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25 The Supporting Information contains the X-ray crystal structures of compounds **2**, **9** and **10**. Crystallographic data for azolium salts **2**, **9** and **32** has been deposited with the Cambridge Crystallographic Data

Centre as supplementary publication numbers CCDC 809724, CCDC 809725 and CCDC 809726.
26 Rearrangement of **15** and **16** using 2 (10 mol%) and $NEt_3$ (100 mol%) gave, at >95% and ~90% conversion, a 75 : 25 and 66 : 34 mixture of carbonate to the corresponding azlactone respectively.
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31 In each case, the crude reaction product contained ~10% of either diethyl phenyl or diethyl 1-naphthyl carbamate **43** or **44**.
32 Monitoring the progress of this two-step domino reaction sequence by $^1H$ NMR spectroscopic analysis commencing from phenylalanine derived azlactone indicated full conversion to oxazolyl carbonate **4** as the sole reaction product after short reaction times (1 to 15 min), with subsequent slow rearrangement of carbonate **4** to give *C*-carboxyl-**5** observed. This reaction profile is consistent with oxazolyl carbonate **4** being an intermediate in this reaction pathway rather than direct C-carboxylation of the azlactone promoted by the NHC generated from precatalyst **2** under the reaction conditions.
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