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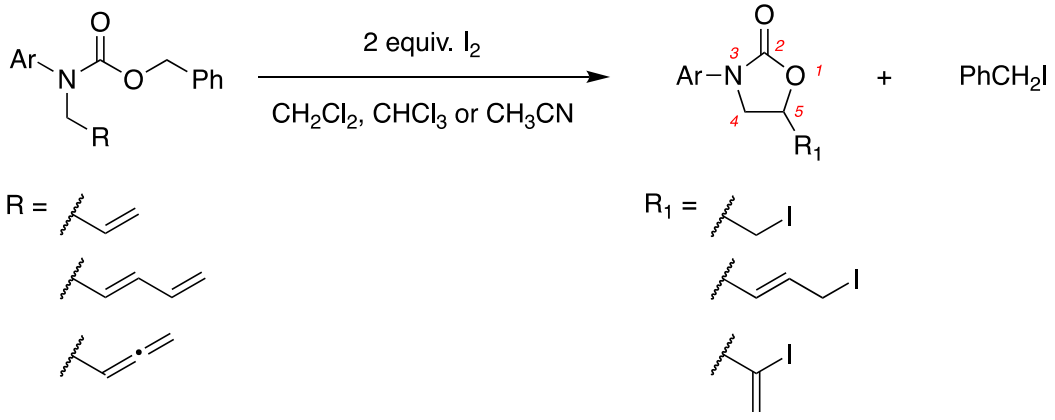


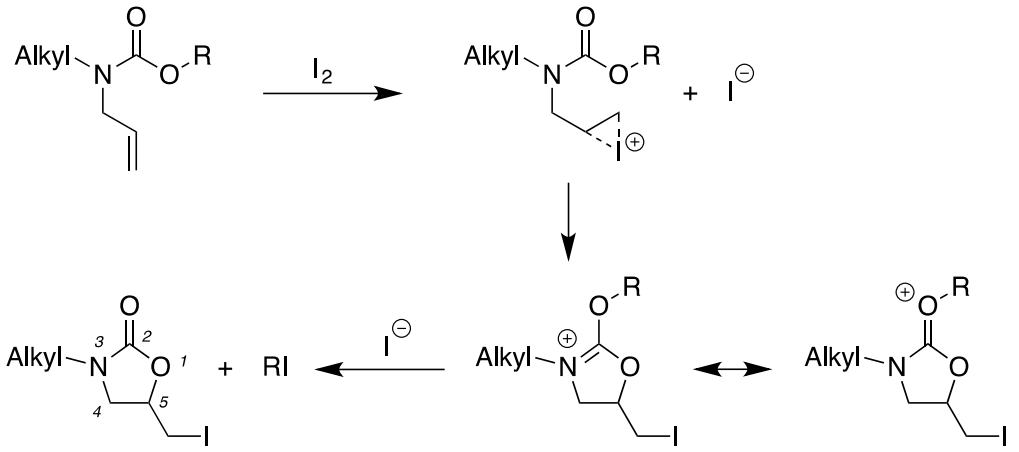
ABSTRACT

3-Aryl- and 3-heteroaryloxazolidin-2-ones, by virtue of the diverse pharmacologic activities exhibited by them after subtle changes to their appended substituents, are becoming increasingly important and should be considered privileged chemical structures. The iodocyclocarbamation reaction has been extensively used to make many 3-alkyl-5-(halomethyl)oxazolidin-2-ones, but the corresponding aromatic congeners have been relatively underexplored. We suggest that racemic 3-aryl- and 3-heteroaryl-5-(iodomethyl)oxazolidin-2-ones, readily prepared by the iodocyclocarbamation reaction of *N*-allylated *N*-aryl or *N*-heteroaryl carbamates, may be useful intermediates for the rapid preparation of potential lead compounds with biological activity. We exemplify this point by using this approach to prepare racemic linezolid, an antibacterial agent. Herein, we report results of our systematic investigation into the scope and limitations of this process and have identified some distinguishing characteristics within the aryl/heteroaryl series. We also describe the first preparation of 3-aryloxazolidin-2-ones bearing new functionalized C-5 substituents derived from conjugated 1,3-dienyl and cumulated 1,2-dienyl carbamate precursors. Finally, we describe the utility of the iodocyclocarbamation reaction for making six-membered tetrahydro-3-aryl-1,3-oxazin-2-ones.

INTRODUCTION

The iodocyclocarbamation reaction of allylic and homoallylic *N*-alkylcarbamates is an effective means of constructing both 3-alkyloxazolidin-2-ones and their 6-membered congeners, the tetrahydro-3-alkyl-1,3-oxazin-2-ones.[1] The utility of this approach was first demonstrated by Pauls and Fraser-Reid as part of their elegant synthesis of the amino sugar garosamine.[2] Subsequent reports continued to expand the usefulness of this type of transformation, but with an almost exclusive focus on iodocyclocarbamation reactions employing *N*-alkyl or *N*-benzyl allylic carbamate substrates (Scheme 1).[3]

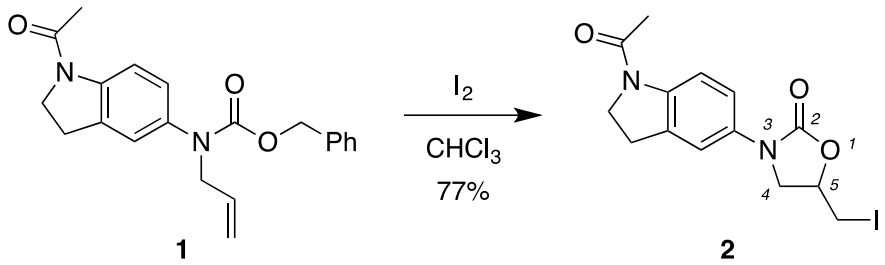
Scheme 1. The Iodocyclocarbamation Reaction of Allylated *N*-Alkyl Carbamates[1,2,3]



Interestingly, allylic carbamate substrates bearing aryl or heteroaryl nitrogen substituents have been largely overlooked. Presumably, this emphasis on iodocyclocarbamation reactions leading to 3-alkyl-5-(iodomethyl)oxazolidin-2-one products reflects a primary focus on chemical intermediates useful for making amino alcohols, via subsequent degradation of the oxazolidinone's carbamate linkage.

The first example of an iodocyclocarbamation reaction involving an allylated *N*-arylcarbamate was reported by Brickner and co-workers and involved the iodine-mediated conversion of *N*-indolinyl allylic carbamate **1** to the corresponding racemic 3-(indolin-5-yl)-5-(iodomethyl)oxazolidin-2-one **2** in 77% isolated yield (Scheme 2).[4] In two subsequent papers, focused on the regioselective metalation of stabase-protected anilines and palladium-mediated cross-coupling reactions with trimethylstannyltropones, the iodocyclocarbamation reaction was briefly described.[5a,b] A few more recent papers describing *N*-4-pyridyl,[6] *N*-3-thienyl,[7] and *N*-1-quinolin-4-yl[8] allylic carbamates as substrates in the iodocyclocarbamation reaction have appeared but, again, generally not as the primary emphasis of the described research. There remains a real need for a more comprehensive examination of *N*-aryl and *N*-heteroaryl carbamates as substrates in the iodocyclocarbamation reaction, with the goal of further defining and expanding the scope and limitations of this important cyclization process.

Scheme 2. Iodocyclocarbamation Reaction of *N*-Allyl *N*-(5-Indolinyl)carbamate 1



1 2

Our interest in further exploring the iodocyclocarbamation reaction was also driven by a recognition of the potential importance of 3-aryl- and 3-heteroaryl-5-(iodomethyl)oxazolidin-2-one products as useful intermediates for the synthesis of a variety of therapeutically useful racemic substances. In fact, the 5-substituted 3-aryl- and 3-heteroaryloxazolidin-2-one motif could be formally considered as a "privileged chemical structure," a term first coined by Evans and co-workers to describe molecular scaffolds that, with slight changes in appended substituents, can express a wide range of discrete therapeutic activities.[9] As exemplars, the marketed pharmaceutical agents linezolid, rivaroxaban, and toloxatone, each incorporating a substituted 3-phenyloxazolidin-2-one core with distinct C-5 side chains, exhibit antibacterial, anticoagulant, and antidepressant activities, respectively (Figure 1).[10,11,12] Additional 3-aryl- and 3-heteroaryloxazolidin-2-ones with substitution at the 5-position have been reported to inhibit or bind HIV-1 protease,[13] glycoprotein (GP-IIb/IIIa),[14] metabotropic glutamate receptor (mGluR),[15] and various calcium channel receptors.[16]

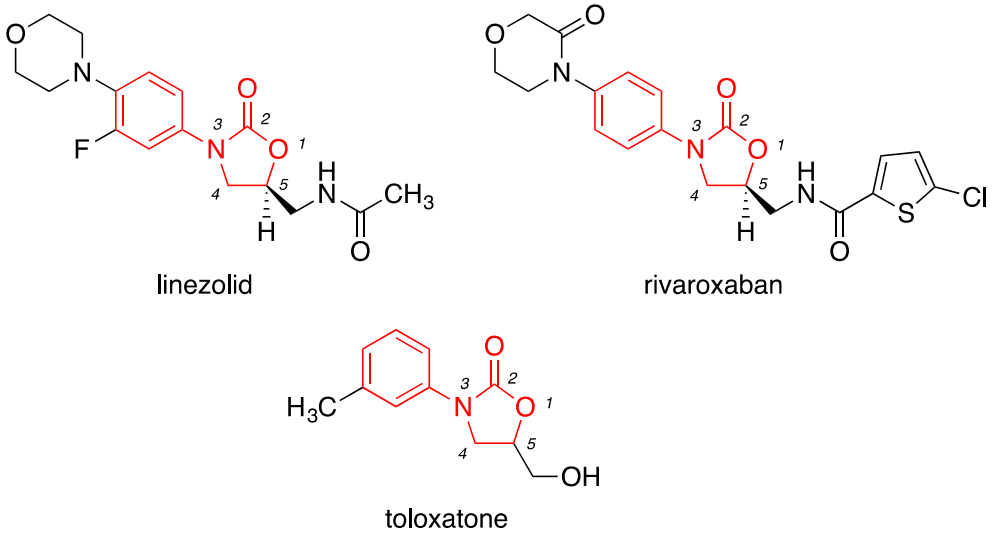


Figure 1. Examples of phenyloxazolidinone "privileged chemical structures."

Taken together, the structural breadth of the therapeutic examples described above suggests a possible synthetic role for the 3-aryl- and 3-heteroaryl-5-(iodomethyl)oxazolidin-2-one products of the iodocyclocarbamation reaction. The primary iodide moiety would certainly be amenable to further synthetic elaboration to provide access to a number of relevant C-5 side chain substituents. The use of allylic carbamate starting materials with an array of aromatic and heteroaromatic appendages on their nitrogen would provide additional structural diversity. Overall, exploitation of the iodocyclocarbamation reaction could enable the rapid synthesis of racemic intermediates with potential to facilitate the identification of new lead compounds. The eventual identification of any interesting compounds would then require a subsequent developmental effort in order to generate these substances in enantiomerically enriched form.

As described herein, while the iodocyclocarbamation reaction generally proceeds in useful yields for a wide variety of 3-aryloxazolidin-2-ones, there was no guarantee of success *a priori* for an expanded survey of the reaction, given the presence of a variety of highly electrophilic species during the course of the reaction (Scheme 1). Iodine and other electrophilic species, such as an iodonium ion intermediate, presented some potential for electrophilic aromatic substitution side reactions, especially

in the presence of a very electron-rich aromatic ring (*e.g.* di- or trimethoxyphenyl or aminophenyl). In addition, given the generation of benzyl iodide from the Cbz carbamates used in the cyclization process, extension of this chemistry to the synthesis of various nitrogen-containing 3-heteroaryloxazolidin-2-ones could potentially be thwarted by untoward alkylation of any basic nitrogen atom(s), both in the case of the starting *N*-allylcarbamate as well as the cyclized product. Indeed, the development of modified reaction conditions to circumvent this problem became crucial for salvaging the applicability of the iodocyclocarbamation reaction to the synthesis of various 3-heteroaryloxazolidin-2-ones, for example the pyridyl derivatives (*vide infra*). Finally, we also share the results of our successful attempts to extend this cyclization chemistry beyond simple allylic carbamate substrates to encompass conjugated *N*-(1,3-pentadien-5-yl) and cumulated *N*-(1,2-butadien-4-yl) carbamate starting materials, affording synthetic entry to oxazolidinones bearing interesting functionalized C-5 side chains poised for further modification. The use of a homoallylic carbamate is also described, providing entry to the corresponding tetrahydro-3-aryl-6-(iodomethyl)-1,3-oxazin-2-one six-membered ring congeners.

RESULTS AND DISCUSSION

Synthesis of *N*-Allyl *N*-carbobenzyloxy Anilines and Heteroarylamines 5. The *N*-aryl and *N*-heteroaryl *O*-benzyl carbamates **4**, required for synthesis of the *N*-allyl carbamate substrates **5**, were prepared in excellent yields via treatment of the requisite commercially available anilines or heteroarylamines **3** with benzyloxy chloroformate (CbzCl), using either Schotten-Baumann conditions with sodium bicarbonate ($NaHCO_3$) in aqueous acetone, or anhydrous conditions with potassium carbonate (K_2CO_3) in THF (Scheme 3). The *N*-allyl *N*-Cbz aromatic amine starting materials **5** for the planned iodocyclocarbamation reactions were most conveniently prepared in our hands by allylation of the *N*-aryl- or *N*-heteroarylcarbamates **4**. This involved deprotonation of **4** with either NaH in THF or cesium carbonate (Cs_2CO_3) in DMF, followed by alkylation with allyl bromide, typically at room

temperature. In most instances, catalytic tetrabutylammonium iodide [(n-Bu)$_4$NI] was added to further facilitate the allylation reaction. In general, the allylated carbamates **5** were isolated as oils or gums in good, sometimes excellent yield after chromatographic purification (Table 1). In some instances, the allylated products **5** were difficult to separate by chromatography from any residual starting material **4**. In these cases, it was critical that the allylation reaction went to completion.

One limitation of this method of allylation became apparent in the attempted alkylation of the 2-aminothiazole-derived Cbz carbamate **7** (Scheme 4). In the event, the allylation reaction afforded a 3:1 ratio of the desired *N*-allyl carbamate **8**, isolated in 72% yield, along with the thiazolylidene side product **9**, resulting from allylation of the thiazole ring nitrogen, in 25% yield. The observed regioselectivity in the allylation of **7** is very similar to the alkylation results reported in the literature for a Boc derivative of 2-aminothiazole.[17]

Scheme 3. Preparation of 3-Aryl- and 3-Heteroaryl-5-(iodomethyl)oxazolidin-2-ones 6

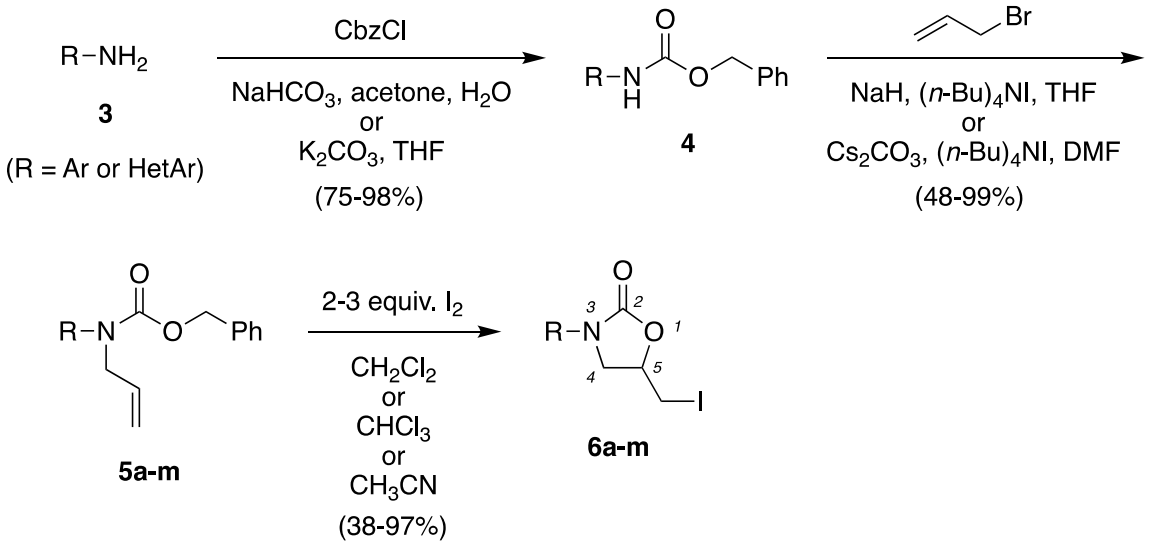
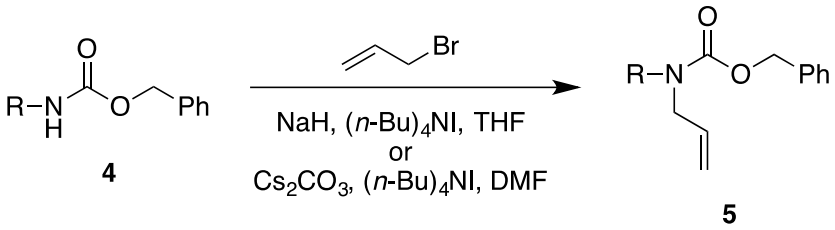


Table 1. Synthesis of Intermediates 5 via Allylation of *N*-Aryl- and *N*-Heteroarylcarbamates 4



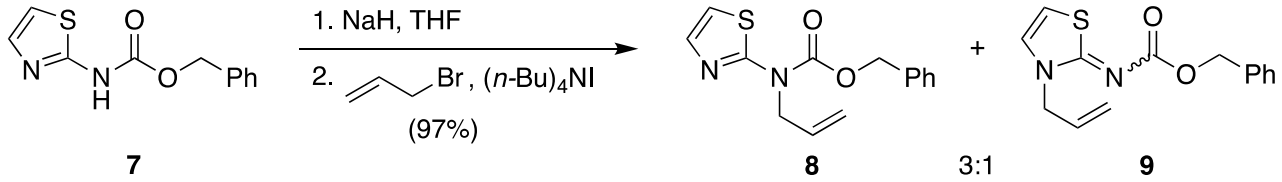
entry	R	conditions[a]	yield (%)[b]
1	C_6H_5 (**5a**)	A	97
2	2-MeC_6H_4 (**5b**)	A	99
3	2,6-$Me_2C_6H_3$ (**5c**)	B	73
4	4-BrC_6H_4 (**5d**)	B	83
5	4-IC_6H_4 (**5e**)	A	96
6	3,4,5-$F_3C_6H_2$ (**5f**)	B	83
7	2,3,4-$F_3C_6H_2$ (**5g**)	A	89
8	3,5-$(CF_3)_2C_6H_3$ (**5h**)	A	85
9	3-F-4-$(NO_2)C_6H_3$ (**5i**)	A	71
10	4-Br-3-$MeOC_6H_3$ (**5j**)	A	48
11	4-MeO-3-$(CF_3)C_6H_3$ (**5k**)	A	69
12	3,4-$(MeO)_2C_6H_3$ (**5l**)	B	96
13	3-fluoro-4-(morpholin-4-yl)C_6H_3 (**5m**)	A	95
14	pyridin-2-yl (**5n**)	A	95
15	pyridin-3-yl (**5o**)	A	75
16	pyridin-4-yl (**5p**)	A	71
17	quinolin-2-yl (**5q**)	A	91

18	quinolin-3-yl (**5r**)	A	90
19	quinolin-6-yl (**5s**)	A	94
20	quinolin-8-yl (**5t**)	A	87

[a]A: 1) NaH, THF, 0 ºC to rt, 2) allyl bromide, (n-Bu)$_4$NI, rt; B: Cs_2CO_3, allyl bromide, (n-Bu)$_4$NI, rt.

[b]Isolated yield.

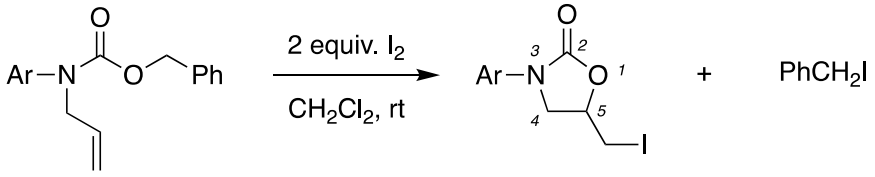
Scheme 4. Allylation of Cbz Carbamate 7 derived from 2-Aminothiazole.



The Iodocyclocarbamation Reaction of *N*-Allylated *N*-Arylcarbamates 5a-m. For our initial investigations into the iodocyclocarbamation reaction of aryl *N*-allyl *O*-benzyl carbamates **5a-m**, we used conditions similar to those utilized by Takano and Ohno for the corresponding alkyl *N*-allyl subtrates.[3d,f] This involved treatment of **5** with 2 equivalents of I_2 in $CHCl_3$ at room temperature (Scheme 3). We also examined CH_2Cl_2 and CH_3CN as alternative solvents and found that they typically provided comparable results. Most of the reactions reported herein were conducted in CH_2Cl_2 ("standard conditions," Table 2). For *N*-aryl substrates **5a-m**, all examples underwent clean iodocyclocarbamation under the standard conditions, providing the targeted racemic 3-aryl-5-(iodomethyl)oxazolidin-2-ones **6a-m** in generally high yield, after purification by chromatography or recrystallization. There was no obvious evidence of any untoward reaction in the synthesis of these substituted 3-aryloxazolidinones. This was somewhat surprising, as we had speculated that very electron-rich aromatic rings, such as the 3,4-dimethoxyphenyl moiety of **5l** (Table 2, entry 12), might be

susceptible to some level of an electrophilic aromatic substitution side reaction due to the presence of the various electrophilic species noted in Scheme 1. This undesired reaction manifold was not observed for any of the aryl systems investigated (**5a-m**).

Table 2. Iodocyclocarbamation of Allylated *N*-Aryl Intermediates to Provide Substituted 3-Phenyl-5-(iodomethyl)oxazolidin-2-ones 6a-m



5a-m **6a-m**

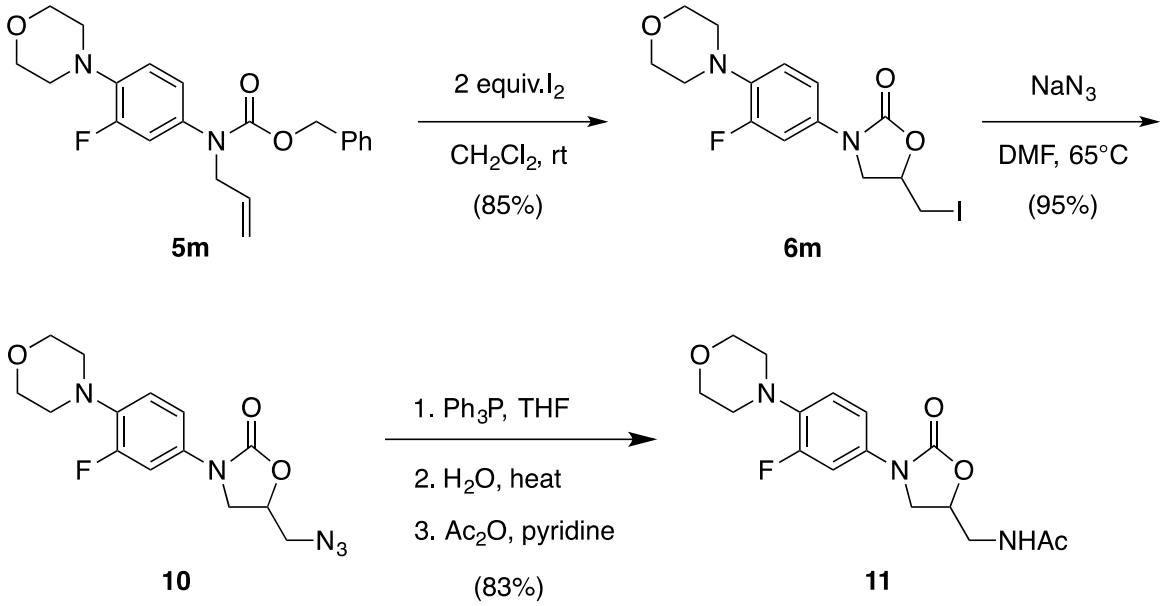
entry	Ar	Yield (%)[a,b]
1	C_6H_5 (**6a**)	97
2	2-MeC_6H_4 (**6b**)	70
3	2,6-$Me_2C_6H_3$ (**6c**)	86
4	4-BrC_6H_4 (**6d**)	95
5	4-IC_6H_4 (**6e**)	94
6	3,4,5-$F_3C_6H_2$ (**6f**)	89
7	2,3,4-$F_3C_6H_2$ (**6g**)	92
8	3,5-$(CF_3)_2C_6H_3$ (**6h**)	78
9	3-F-4-$(NO_2)C_6H_3$ (**6i**)	74
10	4-Br-3-$MeOC_6H_3$ (**6j**)	70
11	4-MeO-3-$(CF_3)C_6H_3$ (**6k**)	73
12	3,4-$(MeO)_2C_6H_3$ (**6l**)	94

13	3-fluoro-4-(morpholin-4-yl)C_6H_3 (**6m**)	85

[a]Standard conditions: 2 equivalents I_2, CH_2Cl_2, rt. [b]Isolated yield.

The iodocyclocarbamation reaction of *N*-allyl *N*-[3-fluoro-4-(morpholin-4-yl)phenyl]carbamate **5m** was found to proceed uneventfully, despite the presence of a weakly basic tertiary amine nitrogen, pK_b = ~8) in its appended morpholine ring, to give the 5-(iodomethyl)oxazolidin-2-one **6m** in 85% isolated yield (Table 2, entry 13). There was no evidence of any alkylation of this nitrogen with benzyl iodide generated during the course of the reaction. Compound **6m** is amenable to further synthetic elaboration (Scheme 5). Nucleophilic displacement of the primary iodide proceeded uneventfully with sodium azide (DMF, 65 °C) to give the 5-(azidomethyl)oxazolidin-2-one **10** in 95% yield after chromatography. A Staudinger reaction, followed by hydrolysis and then acetylation, afforded an 83% isolated yield of (±)-linezolid (**11**), an antibiotic with potent activity against pathogenic Gram-positive bacteria.[10,18]

Scheme 5. Application of the Iodocyclocarbamation Reaction to a Synthesis of the Antibiotic Linezolid in Racemic Form



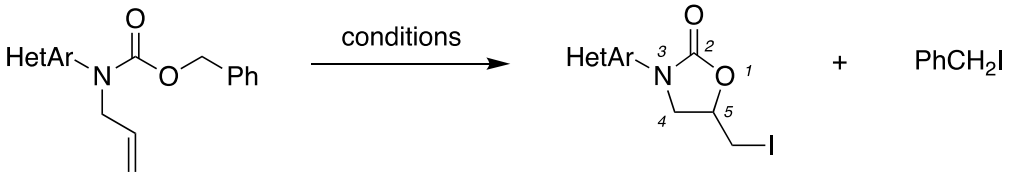
The Iodocyclocarbamation Reaction of *N*-Allylated *N*-Heteroarylcarbamates 5n-t.

The mechanism of the iodocyclocarbamation of allylic O-benzylcarbamates, as depicted in Scheme 1, involves an intramolecular attack of the carbamate's carbonyl oxygen atom on a cyclic iodonium ion, leading to the intermediacy of a benzyl-substituted oxonium ion-iodide ion pair. This presumably collapses via benzylic cleavage by iodide ion, to give one equivalent each of benzyl iodide and the 5-(iodomethyl)oxazolidin-2-one. As noted above, these electrophilic species did not undergo untoward electrophilic aromatic substitution reactions on the aryl rings examined (**5a-m**). However, co-generation of these reactive intermediate alkylating species, along with the by-product benzyl iodide itself, might be expected to represent a serious limitation with various heterocyclic substrates, in particular, *N*-allyl *N*-heteroarylcarbamates bearing a basic nitrogen atom. Indeed, an early application of iodocyclocarbamation reaction conditions to allylated pyridin-3-yl- and pyridin-4-ylphenyl carbamates was reported to completely fail because of significant *N*-benzylation of the basic nitrogen atom in these systems.[5] A measure of success was ultimately achieved in this prior work through the introduction of excess pyridine into the $CHCl_3$-based reaction medium to serve as an effective benzyl iodide scavenger. There remained a need to systematically explore the scope and limitations of this approach, as well as potential alternatives, in the context of the series of *N*-allylated *N*-pyridyl- and *N*-quinolinylcarbamates **5n-t** described herein (Table 1, entries 14-20).

We initially investigated the iodocyclocarbamation reaction of selected *N*-allylated *N*-heteroarylcarbamate congeners **5o**, **5p**, **5r** and **5s** in $CHCl_3$ (or CH_2Cl_2) at rt or reflux temperature in the presence of 2 equivalents of I_2 ("standard conditions," Scheme 3) and found that, in general, only trace amounts of the desired products, **6o**, **6p**, **6r** and **6s** were formed. Some starting material was recovered but the major product was presumably the corresponding *N*-benzyl pyridinium or quinolinium salts. A summary of selected reaction conditions explored and iodocyclocarbamation results obtained is shown in Table 3. The addition of 10 equivalents of pyridine to the standard reaction conditions, in an attempt

to trap the nascent benzyl iodide, generally did not appreciably improve the reaction outcome in either the pyridin-3-yl or quinolin-6-yl series. For example, **5o** afforded only a trace of the cyclized product **6o** (Table 3, entry 1. Similarly, the quinolin-6-yl substrate **5s** provided only a 23% yield of the desired product **6s** (Table 3, entry 8), along with 41% recovered starting material. What did facilitate conversion to the targeted 5-(iodomethyl)oxazolidin-2-one products was the replacement of $CHCl_3$ with CH_3CN in the presence of the same pyridine additive. In this way, a 48% isolated yield of the 5-(iodomethyl)oxazolidin-2-one product **6s** was obtained from **5s** after chromatographic purification (Table 3, entry 9), along with 23% of recovered **5s**. The reason for the potentiating role of CH_3CN in these reactions is not entirely clear but a contributing factor appears to involve some degree of trapping of the generated benzyl iodide by-product, as varying amounts of *N*-benzylacetamide, presumably resulting from a Ritter-like reaction process, are often isolated. Adding a third equivalent of I_2 to the CH_3CN/pyridine system provided a further enhancement, with only a trace of **5s** observed and a 60% yield of the targeted 3-(quinolin-6-yl)oxazolidin-2-one product **6s** now realized (Table 3, entry 10). Application of these optimized conditions to the pyridin-3yl starting material **5o** afforded a 57% isolated yield of the 3-(pyridin-3-yl)oxazolidin-2-one product **6o** (Table 3, entry 2). The introduction of additional I_2 (up to 10 equivalents) led to reduced yields of **6o**. The allylated quinolin-3-yl carbamate **5r**, isoelectronic with the pyridin-3-yl system, also underwent smooth cyclization to the corresponding 5-(iodomethyl)-3-(quinolin-3-yl)oxazolidin-2-one product **6r** in 64% yield (Table 3, entry 7). Application of the optimized CH_3CN/pyridine-based conditions to the pyridin-4-yl substrate **5p** afforded the desired product **6p**, but in a more modest yield of only 38% (Table 3, entry 6). It should be noted that Chung and co-workers previously reported the iodocyclocarbamation of **5p** in $CHCl_3$/pyridine but obtained only a 19% yield of **6p**.[6]

Table 3. Iodocyclocarbamation of Allylated *N*-Heteroaryl Intermediates 5o-p, r-s to Provide Substituted 3-Heteroaryl-5-(iodomethyl)oxazolidin-2-ones 6o-p, r-s



5o-p, **r-s** **6o-p**, **r-s**

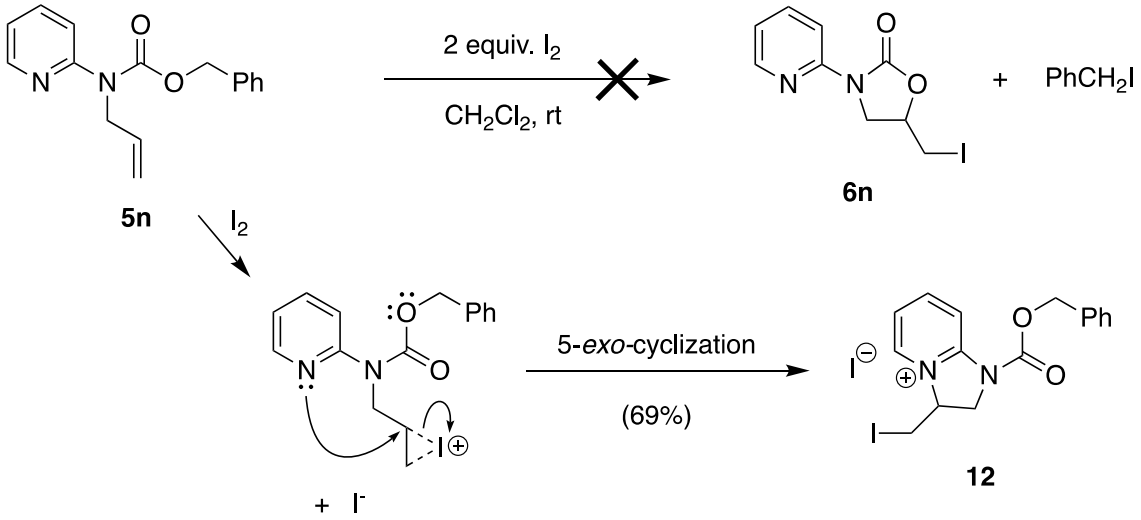
Entry	HetAr	Solvent	Temp (°C)	Time (h)	Equiv. I_2	Equiv. Py	Yield (%)[a]
1	pyridin-3-yl (**6o**)	$CHCl_3$	25	60	2	10	trace
2	pyridin-3-yl (**6o**)	CH_3CN	81	24	3	10	57
3	pyridin-4-yl (**6p**)	$CHCl_3$	25/61	24	2	10	trace
4	pyridin-4-yl (**6p**)	CH_2Cl_2	25	48	2	10	trace
5	pyridin-4-yl (**6p**)	CH_3CN	70	48	2	10	24
6	pyridin-4-yl (**6p**)	CH_3CN	81	24	3	10	38
7	quinolin-3-yl (**6r**)	CH_3CN	81	27	3	10	64
8	quinolin-6-yl (**6s**)	$CHCl_3$	60	15	2	10	23
9	quinolin-6-yl (**6s**)	CH_3CN	81	17	2	10	48
10	quinolin-6-yl (**6s**)	CH_3CN	81	22	3	10	60

[a]Isolated yield.

Based on the mechanism of the iodocyclocarbamation reaction, we anticipated some challenges in translating the *N*-allylated *N*-pyridin-2-yl carbamate **5n** to the targeted 5-(iodomethyl)oxazolidin-2-one product **6n** because of the close proximity of its basic pyridine nitrogen atom to the nascent iodonium ion intermediate (Scheme 6). Indeed, reaction of **5n** with I_2 under a variety of conditions led exclusively to a new, much more polar UV-active product which was not **6n** but rather, as subsequent

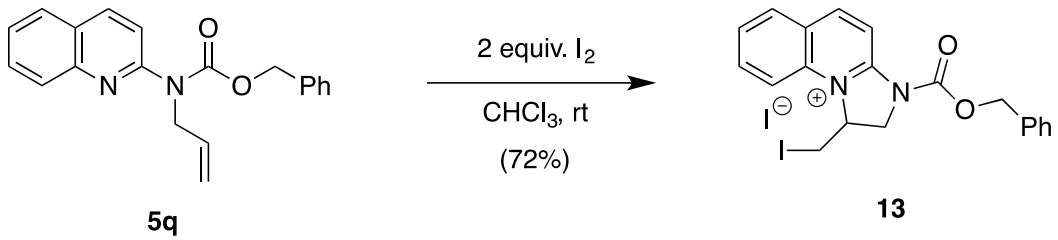
analysis would reveal, the cyclized pyridinium salt **12**. Remarkably, **12** survived an extractive workup with aqueous sodium thiosulfate to provide, after precipitation from the partially concentrated CH_2Cl_2 organic phase, a reasonably clean solid. Recrystallization from toluene/methanol afforded a 69% isolated yield of **12** as a white crystalline solid. The NMR spectral data for **12** was consistent with the assigned structure and this finding was unequivocally confirmed by a single-crystal X-ray structure determination (Figure S1 in the Supporting Information).

Scheme 6. Attempted Preparation of 5-(Iodomethyl)oxazolidin-2-one 6n via Iodocyclocarbamation Reaction of 5n

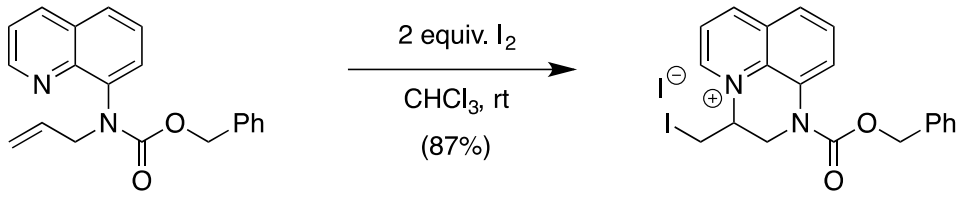


By analogy to the results obtained for **5n**, the *N*-allyl *N*-quinolin-2-yl and *N*-allyl *N*-quinolin-8-yl carbamates **5q** and **5t**, respectively, would also be expected to form cyclic quinolinium salts upon treatment with I_2 under the usual iodocyclocarbamation conditions (Scheme 7). In the event, carbamate **5q** afforded, after recrystallization, a 72% isolated yield of tricyclic quinolinium salt **13**. Similarly, the tricyclic quinolinium salt **14** was efficiently obtained in 87% recrystallized yield via a 6-*exo* cyclization process from precursor **5t**.

Scheme 7. Formation of Cyclic Quinolinium Salts 13 and 14 from Precursors 5q and 5t, Respectively



5q **13**

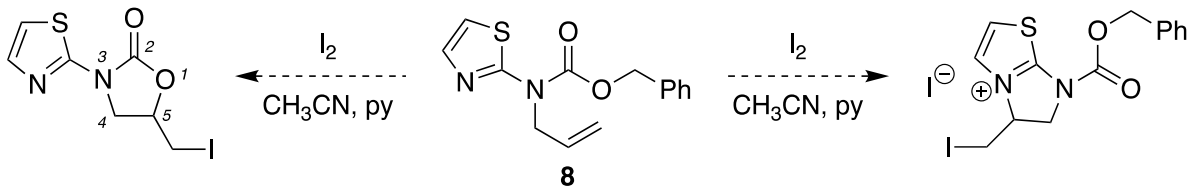


5t **14**

Attempted Iodocyclocarbamation Reaction of *N*-Allylated *N*-Thiazolylcarbamate 8.

We subjected the aforementioned *N*-allyl-*N*-(benzyloxycarbonyl)-2-aminothiazole (**8**, Scheme 4) to the optimized iodocyclocarbamation reaction conditions used in the above-described pyridyl and quinolyl series in an attempt to generate a 3-thiazolyl-oxazolidin-2-one product (Scheme 8). While **8** was consumed, there was no evidence for any oxazolidinone ring formation; presence of an oxazolidinone is easily determined via the consistency of oxazolidinone C-4 and C-5 ^{1}H NMR signals and their associated multiplicities. There was also no formation of the other possible predicted product, a cyclic thiazolium salt analogous to what we obtained previously in the 2-aminopyridine, 2-aminoquinoline and 8-aminoquinoline series (see Schemes 6 and 7). In short, the thiazole ring system does not appear to be a good substrate for the iodocyclocarbamation reaction.

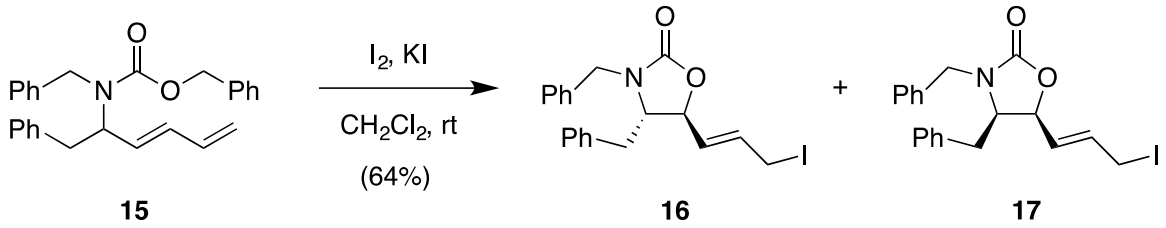
Scheme 8. Attempted Iodocyclocarbamation of 8



8

Extension of the Iodocyclocarbamation Reaction to a Conjugated *N*-1,3-Pentadien-5-yl Carbamate System. Conceptually, extension of the *N*-allyl iodocyclocarbamation reaction to an extended conjugated diene system would be desirable. In the parallel *N*-alkyl series, Takemoto and co-workers previously described the iodocyclocarbamation reaction of, for example, *N*-1,3-pentadien-5-benzyl-5-yl *N*-benzyl carbamate **15** (Scheme 9).[19] Conversion of **15** to 4,5-disubstituted oxazolidin-2-one isomers **16** and **17**, in a combined yield of 64%, proceeded with good regioselectivity and a measure of stereoselectivity (63:37, respectively). Notably, no *N*-aryl or *N*-heteroaryl carbamates were reported. In addition, their carbamate substrates were made via a multi-step synthesis involving, as starting materials, (tricarbonyl)iron complexes of various dienes.

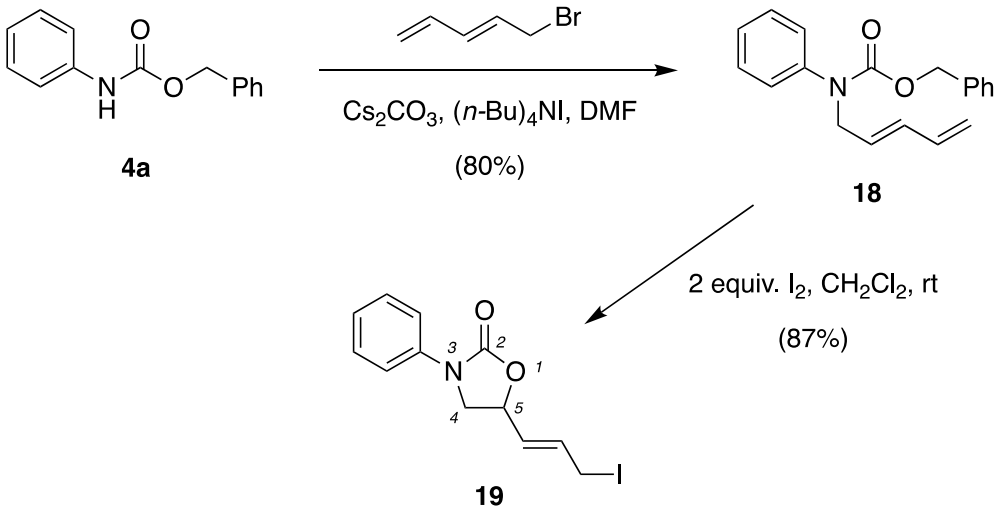
Scheme 9. Iodocyclocarbamation of Substituted *N*-(1,3-Butadienyl)methyl Carbamate 15[19]



Returning to *N*-aryl substrates, the principal focus of this research, we envisioned a simple alkylation strategy to construct the initial *N*-1,3-pentadien-5-yl carbamate substrate **18** (Scheme 10). To that end, aniline-derived carbamate **4a** was reacted with easily prepared 5-bromo-1,3-pentadiene[20] in the presence of $(n\text{-Bu})_4NI$ and Cs_2CO_3 in DMF to give the desired dienyl carbamate **18** in 80% isolated yield. When substrate **18** was treated under the "standard" iodocyclocarbamation conditions (2 equiv. I_2, CH_2Cl_2, rt) we were pleased to see that the 5-*exo* cyclization product **19** was formed in 87% yield after chromatographic purification. The double bond of **19** was assigned the *trans* configuration based on the observed coupling constant of 15.1 Hz in its ^1H NMR spectrum. The functionalized 3-iodopropen-1-yl C-5 side chain of **19** should be a useful synthetic "handle" for rapidly integrating additional structural diversity into this privileged 3-aryloxazolidin-2-one structure. Extending this chemistry to heteroaryl

systems containing a basic nitrogen atom may be a challenge because of the intrinsic reactivity of the C-5 allylic iodide moiety.

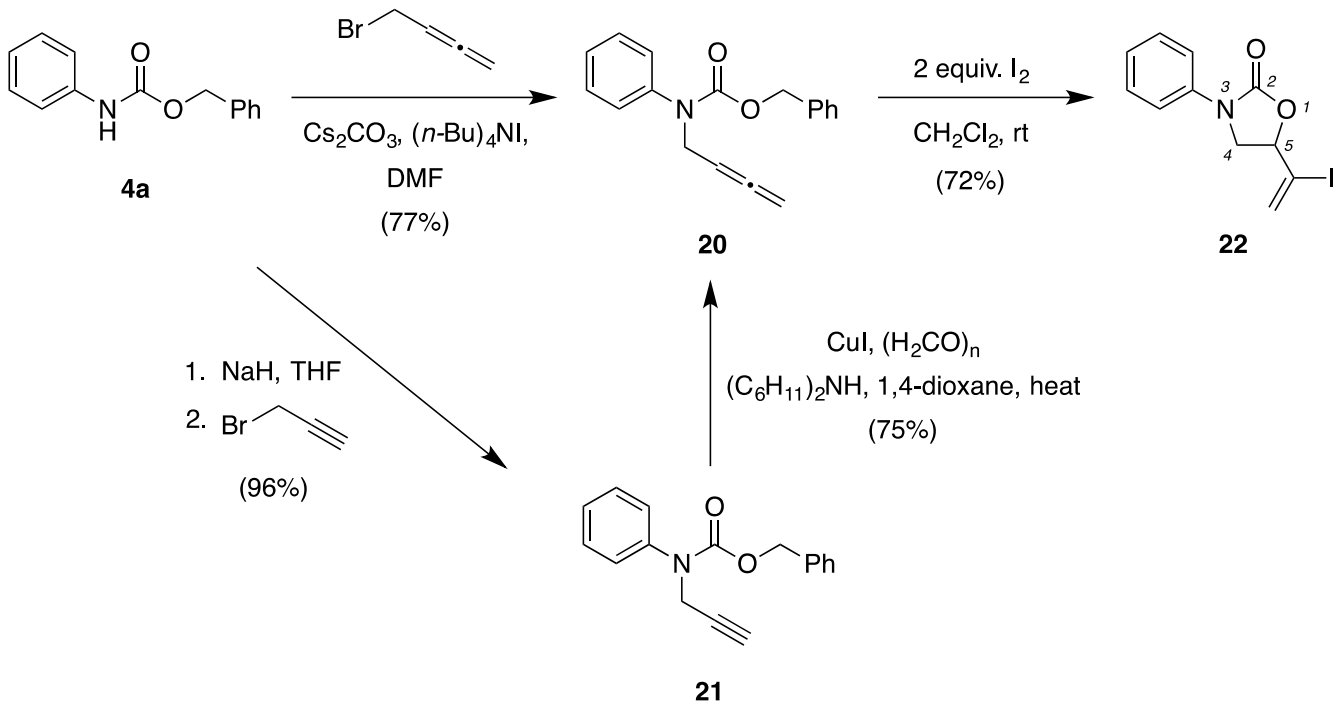
Scheme 10. Preparation and Iodocyclocarbamation Reaction of *N*-1,3-Pentadien-5-yl *N*-Phenyl Carbamate 18 to Give 5-(3-iodoprop-1-en-1-yl)oxazolidin-2-one 19



Extension of the Iodocyclocarbamation Reaction to a Cumulated *N*-1,2-Butadien-4-yl Carbamate Substrate. We were also interested in exploring the possibility of using a cumulated diene appendage on the starting carbamate nitrogen in order to access alternative functionality, namely a vinyl iodide, on the C-5 side chain of the oxazolidinone product. As shown in Scheme 11, we approached the synthesis of the key *N*-1,2-butadien-4-yl carbamate **20** via two different routes. In the first of these, *N*-alkylation of carbamate **4a** with 4-bromo-1,2-butadiene[21,22] was achieved with Cs_2CO_3 and $(n\text{-Bu})_4NI$ in DMF to afford **20** in 77% yield. A second and preferable approach involved deprotonation of **4a** with NaH in THF or DMF, followed by alkylation with propargyl bromide, to provide the *N*-propargyl carbamate derivative **21** in 96% yield. Compound **21** was then subjected to a Crabbé homologation with paraformaldehyde in the presence of CuI, $(C_6H_{11})_2NH$ and 1,4-dioxane, with heating, to give the same *N*-allenylmethyl derivative **20** in 75% isolated yield.[23] Compound **20** exhibited a signal in its ^{13}C NMR spectrum at 208.9 ppm, characteristic of the central carbon of an allene moiety.[24] Intermediate **20** was

treated with two equivalents of I_2 in CH_2Cl_2 at rt to give, after workup and chromatographic purification, 72% of the desired 5-(1-iodoethen-1-yl)-3-phenyloxazolidin-2-one **22** along with 13% of recovered **20**. Attempts to increase the conversion by adding a third equivalent of I_2 led to a somewhat lower yield (63%) of the desired product. The ^{1}H NMR spectrum of **22**, which shows two alkene protons at 6.6 and 6.0 ppm, each with small 2 Hz germinal coupling constants, is consistent with the assigned structure. Further, signals for the individual protons at C-4 and C-5 all appear as inter-related doublets of doublets, consistent with formation of the oxazolidinone ring system. This approach should be fully compatible with heteroaryl-substituted starting materials. In addition, the C-5 vinyl iodide side chain of **22** should be amenable to further synthetic manipulation, for example Suzuki-Miyaura cross-coupling reactions.

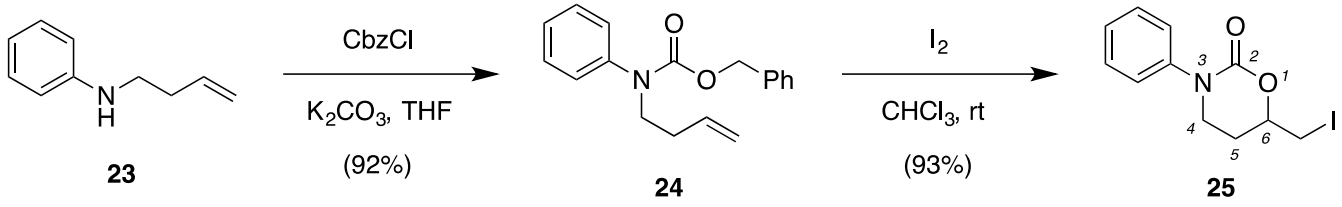
Scheme 11. Preparation and Iodocyclocarbamation Reaction of *N*-1,2-Butadien-4-yl *N*-Phenyl Carbamate 20 to Give 5-(1-Iodoethen-1-yl)oxazolidin-2-one 22



Access to Six-membered Tetrahydro-3-aryl-6-(iodomethyl)-1,3-oxazin-2-ones via the Iodocyclocarbamation Reaction. While the previously described chemistry permits rapid access to

five-membered ring oxazolidinones, it would be desirable to gain entry to the corresponding six-membered ring system, the tetrahydro-3-aryl-6-(iodomethyl)-1,3-oxazin-2-ones (Scheme 12). As a preliminary test case, the starting *N*-(1-buten-4-yl)aniline **23**, obtained by alkylation of aniline with 4-bromo-1-butene,[25] was converted to the Cbz derivative **24** with CbzCl and K_2CO_3 in anhydrous THF in 92% yield. Treatment of the unsaturated carbamate **24** with I_2 ($CHCl_3$, rt) initiated a facile 6-*exo* cyclization to give the racemic tetrahydro-6-(iodomethyl)-3-phenyl-1,3-oxazin-2-one **25** in 93% isolated yield. While not yet explored, the iodocyclocarbamation reaction of heteroaryl versions of **24** to give 3-heteroaryl-1,3-oxazin-2ones should be possible by applying optimized conditions developed for the pyridyl and quinolyl oxazolidinone series described above. Attempts to extend this chemistry further, to enable the synthesis of seven-membered cyclic carbamates, were unsuccessful, as complex mixtures of products were obtained (data not shown).

Scheme 12. Preparation of Tetrahydro-6-(Iodomethyl)-3-phenyl-1,3-oxazin-2-one 25 via an Iodocyclocarbamation Reaction



CONCLUSIONS

In summary, the iodocyclocarbamation reaction of *N*-allylated *N*-aryl- and *N*-heteroarylcarbamates is an efficient, versatile and useful method for the synthesis of racemic 3-aryl- and 3-heteroaryl-5-(iodomethyl)oxazolidin-2-ones. The electron-rich aromatic rings examined, such as the 3,4-dimethoxyphenyl or 4-morpholinylphenyl moieties, did not produce any by-products resulting from an electrophilic aromatic substitution reaction with any of the various electrophilic species present in the iodocyclocarbamation reaction mixture. Heteroaryl systems incorporating a basic nitrogen required

modified conditions involving the use of additional I_2 and an acetonitrile/pyridine co-solvent system to avoid untoward alkylation of the reactive nitrogen. When a heteroaryl basic nitrogen is present in an orientation favoring attack on the intermediate iodonium ion, a different reaction pathway is followed wherein cyclic ammonium salts are generated (e.g. **12**, **13** and **14**). Also, when the allylated thiazole-derived carbamate **8** was subjected to the iodocyclocarbamation reaction conditions, it did not afford predicted or well-characterized reaction products and further investigation is needed to clarify its chemistry. The successfully synthesized 5-(iodomethyl)oxazolidin-2-one products bear useful functionality for making a variety of pharmacologically active substances, as exemplified by the synthesis of the antibacterial agent linezolid in racemic form. Access to alternative oxazolidinone C-5 side chains, such as the 3-iodoprop-1-en-1-yl and 1-iodoethen-1-yl groups, prepared from *N*-1,3-pentadien-5-yl and *N*-1,2-butadien-4-yl carbamates, respectively, are also within scope of this approach. These functionalized side chains should facilitate the incorporation of additional diversity elements into the C-5 position of these privileged chemical structures. We also found that *N*-aryl-*N*-(1-buten-4-yl) carbamates react under standard cyclocarbamation conditions to form the interesting racemic six-membered tetrahydro-3-aryl-6-(iodomethyl)-1,3-oxazin-2-ones. Overall, we envision the *N*-aryl- and *N*-heteroaryl variation of the iodocyclocarbamation reaction as having great potential to expeditiously construct a variety of racemic compounds which could facilitate the identification of new lead substances in various bioactivity screens. Upon such identification, subsequent development activities would then address their preparation in enantiomerically enriched form. The most promising path to enantiomerically enriched iodocyclocarbamation products would seem to be through an eventual application of methodology involving chiral hypervalent iodine catalysts. The pioneering and ongoing work in this area by Denmark, Wirth and Muñiz, amongst others, would seem to have considerable potential as a solution to this problem.[26]

EXPERIMENTAL SECTION

General Considerations. All commercially available solvents and reagents were used without further purification, unless otherwise noted. Starting *N*-aryl and *N*-heteroaryl *O*-benzylcarbamates **4a-t** were commercially available, synthesized from commercially available anilines (**4f**, **4h**), or prepared via Schotten-Baumann reactions as previously described: **4j**,[27] **4k**,[28] **4n**,[29] **4o**,[30] **4p**,[6] **4q**,[31] **4r**,[32] and **4s**.[33] All moisture-sensitive reactions were conducted under a nitrogen atmosphere in oven- or flame-dried glassware. All reactions requiring heating were conducted with a temperature-controlled oil bath. Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were obtained on 400 or 500 MHz NMR spectrometers. Multiplicity is indicated as follows: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); dd (doublet of doublets); dt (doublet of triplets); ddd (doublet of doublet of doublets); qt (quartet of triplets); app (apparent). Chemical shifts (δ) are reported in ppm relative to $CDCl_3$ or TMS. Coupling constants (J) are reported in Hz. IR spectra were obtained on a FT-IR spectrometer. High-resolution mass spectra (HRMS) were obtained on a mass spectrometer operating in ESI (positive or negative) or APCI (positive) modes (TOF mass analysis). Data are reported in the form *m/z* (relative intensity). Analytical TLC was performed on silica gel plates with visualization generally accomplished by UV light (254 nm). Flash chromatography was performed on silica gel (230-400 mesh). Organic solutions were concentrated using a rotary evaporator under reduced pressure unless otherwise stated. For the single crystal X-ray crystallographic study, a colorless needle-shaped crystal of compound **12** with dimensions 0.35×0.06×0.06 mm^3 was mounted on a nylon loop with paratone oil. Data were collected using a Bruker APEX-II CCD diffractometer equipped with an Oxford Cryosystems low-temperature device, operating at T = 173(2) K. Data were measured using ω of -0.50° per frame for 25.09 s using MoK_α radiation (sealed

tube, 50 kV, 40 mA). The total number of runs and images was based on the strategy calculation from the program COSMO (BRUKER, V1.61, 2009).[34] The actually achieved resolution was Θ = 25.374. Cell parameters were retrieved using the SAINT (Bruker, V8.34A, 2013) software and refined using SAINT (Bruker, V8.34A, 2013) on 9540 reflections, 20 % of the observed reflections.[35] Data reduction was performed using the SAINT (Bruker, V8.34A, 2013) software, which corrects for Lorentz polarization. The final completeness is 100.00 out to 25.374 in Θ. The absorption coefficient μ of this material is 3.113 at this wavelength (λ = 0.71073) and the minimum and maximum transmissions are 0.4921 and 0.9478. The structure was solved in the space group $Pca2_1$ (# 29) by Intrinsic Phasing with the ShelXT structure solution program.[36] The structure was refined by Least Squares using version 2014/6 of XL[37] incorporated in Olex2.[38] All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model.

General Procedure for the Preparation of *O*-Benzyl Carbamates 4. *Method A*. A mixture of the aryl amine (60.00 mmol) and $NaHCO_3$ (10.08 g, 120.00 mmol) in water (125 mL) and acetone (250 mL) was cooled to 0 °C, and then treated with benzyl chloroformate (12.28 g, 10.28 mL, 72.00 mmol) over 10 min. The mixture was stirred for 1 h at 0 °C and then the cooling bath was removed. Stirring was continued at ambient temperature overnight. Most of the acetone was then removed by rotary evaporation under reduced pressure and the remaining mixture poured into water (200 mL) and extracted with either EtOAc or CH_2Cl_2. The combined organic extracts were washed with saturated aq. $NaHCO_3$, followed by brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude residue was then purified by recrystallization or silica gel chromatography to provide the title carbamate in excellent yield.

Method B. To dry THF (40 mL) under argon or nitrogen was added the aryl amine (6.65 mmol), powdered K_2CO_3 (1.06 g, 7.68 mmol), and, dropwise, benzyl chloroformate (1.19 g, 1.00 mL, 6.98

mmol). After stirring overnight at ambient temperature, the bulk of the solvent was removed by rotary evaporation under reduced pressure. The resulting paste or solid residue was combined with toluene (50 mL) and the mixture heated to boiling and then filtered gravitationally while hot. Upon cooling, the desired title carbamate typically crystallized from the solution, was isolated by vacuum filtration, and dried under reduced pressure to give good yields of the desired material. In some cases, a second crop was pursued or, alternatively, the filtrate was concentrated under reduced pressure and purified by chromatography over silica gel to provide additional title compound.

Benzyl *N*-(3,4,5-trifluorophenyl)carbamate (4f). Prepared using Method A. White solid (1.125 g, 98%): mp 93-96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 5H), 7.07-7.10 (m, 2H), 6.71 (s, 1H), 5.19 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.9, 152.5, 152.5, 152.4, 152.4, 150.1, 150.0, 150.0, 149.9,137.3, 137.2, 137.0, 135.4, 134.9, 134.7, 134.6, 133.6, 133.6, 133.5, 133.5, 133.4, 133.4, 128.7, 128.6, 128.4, 103.1, 102.8, 67.5; IR (neat) 3323, 3067, 2959, 1706, 1627, 1544, 1433, 1249, 1042 cm^{-1}; HRMS (ESI) m/z: $[M - H]^+$ Calcd for $C_{14}H_9F_3NO_2$ 280.0585; Found 280.0593.

Benzyl *N*-[3,5-bis-(trifluoromethyl)phenyl]carbamate (4h). Prepared using Method A. White solid (1.144 g, 75%): mp 92-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 2H), 7.56 (s, 1H), 7.37-7.41 (m, 5H), 6.96 (s, 1H), 5.24 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.9, 139.3, 135.3, 132.8, 132.6, 132.3, 132.0, 128.7, 128.7, 128.6, 128.4, 127.7, 127.0, 126.3, 124.1, 122.0, 118.3, 116.8, 67.7; IR (neat) 3318, 3108, 1710, 1553, 1388, 1280, 1223, 1179, 1134 cm^{-1}; HRMS (ESI) m/z: $[M - H]^+$ Calcd for $C_{16}H_{10}F_6NO_2$ 362.0616; Found 362.0618.

General Procedure for the Synthesis of *N*-Allyl Carbamates 5. *Method A.* To a cooled (0 °C) solution of the aryl or heteroaryl carbamate (5.00 mmol) in dry THF (50 mL) under N_2 was added NaH (60% dispersion in mineral oil, 0.220 g, 5.50 mmol) in small portions. After stirring for 30-60 min under N_2 the reaction mixture was first treated with *n*-Bu_4NI (0.185 g, 0.50 mmol) and then with allyl bromide

(0.617 g, 0.441 mL, 5.10 mmol). The cooling bath was then removed and the reaction mixture stirred at ambient temperature until TLC analysis (hexane/EtOAc) revealed the reaction to be complete. The reaction mixture was then cooled (0 °C) and carefully treated with H_2O (2 mL) to quench any unreacted NaH. The mixture was transferred to a separatory funnel with CH_2Cl_2 (100 mL) and washed with H_2O (2 x 50 mL) and brine (50 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude allylated product. Chromatography on silica gel, eluting with hexane/EtOAc, afforded, after combining appropriate fractions and concentration under reduced pressure, generally high yields of the targeted allylated product.

Method B. To a solution of the aryl or heteroaryl carbamate (1.37 mmol) in dry DMF (20 mL) under N_2 was added $CsCO_3$ (1.341 g, 4.11 mmol), *n*-Bu_4NI (0.051 g, 0.14 mmol) and then allyl bromide (0.498 g, 0.356 mL, 4.11 mmol). The resultant mixture was warmed to 40 °C and stirred under N_2 until TLC analysis (hexane/EtOAc) revealed the reaction to be complete. The reaction mixture was cooled to ambient temperature, treated with H_2O (44 mL), and then extracted with 1:1 hexane/Et_2O (3 x 100 mL). The combined organic extracts were washed once with H_2O and brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude allylated product. Chromatography on` silica gel, eluting with hexane/EtOAc, afforded, after combining appropriate fractions and concentration under reduced pressure, generally high yields of the targeted allylated product.

***N*-Allyl-*N*-(benzyloxycarbonyl)aniline (5a)** (Method A): oil (1.332 g, 97%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.35 (m, 10H), 5.85-5.95 (m, 1H), 5.16 (s, 2H), 5.11-5.16 (m, 2H), 4.27 (d, J = 5.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.2, 136.6, 133.7, 128.8, 128.4, 127.8, 127.6, 126.8, 126.5, 117.1, 67.2, 53.3; IR (neat) 3064, 3033, 2952, 1706, 1598, 1496, 1398, 1275, 1230, 1145, 1019 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{18}NO_2$ 268.1338; Found 268.1344.

***N*-Allyl-*N*-(benzyloxycarbonyl)-2-methylaniline (5b)** (Method A): oil (mixture of rotamers, 0.645 g, 99%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08-7.42 (m, 9H), 5.87-5.97, (m, 1H), 5.05-5.23, (m, 4H), 4.40 (dd, J = 6.0 and 7.1 Hz, 1H), 3.94 (dd, J = 6.7 and 6.8 Hz, 1H), 2.14, 2.22 (s, s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.4. 140.1, 136.8, 136.0, 133.2, 130.8, 128.4, 128.3, 127.7, 127.6, 127.4, 126.5, 118.1, 67.0, 53.1, 31.0, 17.7; IR (neat) 3067, 3032, 2952, 2925, 2853, 1705, 1602, 1583, 1494, 1399, 1297, 1276, 1148, 1017 cm^{-1}; HMRS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{20}NO_2$ 282.1494; Found 282.1497.

***N*-Allyl-*N*-(benzyloxycarbonyl)-2,6-dimethylaniline (5c)** (Method B): oil (mixture of rotamers, 0.320 g, 73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 – 7.43 (m, 8H), 5.89 – 6.00 (m, 1H), 5.02 – 5.23 (m, 4H), 4.09 (dd, J = 7.8 and 7.8 Hz, 2H), 2.13, 2.19 (ss, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.4, 139.1, 136.8, 136.2, 136.1, 133.6, 133.2, 128.6, 128.5, 128.3, 128.2, 128.0, 127.9, 127.7, 127.6, 127.5, 127.4, 118.3, 118.1, 67.3, 66.9, 53.0, 52.8, 29.7, 18.4; IR (neat) 3067, 3032, 2956, 2925, 1704, 1396, 1295, 1280, 1145, 1011 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}NO_2$ 296.1650; Found 296.1657.

***N*-Allyl-*N*-(benzyloxycarbonyl)-4-bromoaniline (5d)** (Method B): oil (0.190 g, 83%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.8 Hz, 2H) 7.25 – 7.35 (m, 5H), 7.11 (d, J = 7.8 Hz, 2H) 5.83 – 5.92 (m, 1H), 5.10 – 5.16 (m, 4H), 4.09 (d, J = 5.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.9, 136.3, 133.4, 131.9, 128.4, 128.0, 127.8, 125.5, 117.4, 105.0, 67.5, 53.1; IR (neat) 3087, 3067, 3033, 1710, 1643, 1587, 1491, 1392, 1282, 1231, 1147, 1009 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{17}BrNO_2$ 346.0443; Found 346.0449.

***N*-Allyl-*N*-(benzyloxycarbonyl)-4-iodoaniline (5e)** (Method A): oil (0.267 g, 96%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 -7.65 (m, 2H), 7.25 – 7.35 (m, 5H), 6.99 (d, J = 8.1 Hz, 2H), 5.82 – 5.92 (m, 1H), 5.10 – 5.16 (m, 4H), 4.25 (d, J = 4.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.9, 141.8, 137.9,

136.3, 133.4, 128.5, 128.0, 127.8, 117.4, 67.5 53.1, IR (neat) 3063, 3032, 2922, 2849, 1706, 1584, 1487, 1407, 1388, 1280, 1229, 1146, 1005 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{17}INO_2$ 394.0304; Found 394.0310.

***N*-Allyl-*N*-(benzyloxycarbonyl)-3,4,5-trifluoroaniline (5f)** (Method B): oil (0.475 g, 83%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 -7.36 (m, 5H), 6.93 (br s, 2H), 5.82 – 5.91 (m, 1H), 5.12 - 5.19 (m, 4H), 4.24 (d, J = 5.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.6, 152.1, 152.0, 151.9, 151.8, 149.6, 149.5, 149.4, 149.4, 135.9, 132.9, 128.5, 128.2, 127.9, 117.7, 111.0, 67.9, 53.0; IR (neat) 3087, 3068, 3036, 2952, 1712, 1622, 1529, 1449, 1409, 1326, 1234, 1143, 1046 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}F_3NO_2$ 322.1055; Found 322.1059.

***N*-Allyl-*N*-(benzyloxycarbonyl)-2,3,4-trifluoroaniline (5g)** (Method A): oil (0.954 g, 89%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 - 7.40 (m, 5H), 6.90 - 6.96 (m, 2H), 5.82 – 5.92 (m, 1H), 5.10 - 5.15 (m, 4H), 4.25 (d, J = 5.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.8, 151.6, 151.5, 149.1, 148.9, 136.1, 132.7, 128.5, 128.1, 127.5, 123.4, 123.4, 123.3, 123.3, 118.5, 118.4, 111.5, 67.8, 53.0; IR (neat) 3087, 3067, 3036, 2956, 2925, 2853, 1714, 1614, 1514, 1498, 1402, 1306, 1242, 1149, 1021 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}F_3NO_2$ 322.1055; Found 322.1060.

***N*-Allyl-*N*-(benzyloxycarbonyl)-3,5-bis(trifluoromethyl)aniline (5h)** (Method A): oil (1.106 g, 85%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 2H) 7.72 (s, 1H), 7.30 – 7.38 (m, 5H), 5.89 – 5.99 (m, 1H), 5.18 - 5.24 (m, 4H), 4.38 (d, J = 5.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.4, 146.9, 143.7, 135.7, 132.9, 132.6, 132.3, 131.9, 131.6, 128.5, 128.3, 128.0, 126.0, 124.4, 121.7, 119.4, 117.8, 68.1, 52.7; IR (neat) 3091, 3069, 3035, 2956, 1716, 1618, 1472, 1398, 1342, 1278, 1261, 1182, 1137, 1045 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{16}F_6NO_2$ 404.1085; Found 404.1093.

***N*-Allyl-*N*-(benzyloxycarbonyl)-3-fluoro-4-nitroaniline (5i)** (Method A): oil (0.284 g, 71%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (t, J = 8.7 Hz, 1H) 7.33 (s, 6H), 7.23 (d, J = 9.0 Hz, 1H), 5.83 – 5.92 (m, 1H), 5.13 - 5.21 (m, 4H), 4.36 (br s, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 156.8, 154.7, 154.1, 149.0, 135.4, 132.6, 128.7, 128.5, 128.2, 126.4, 119.7, 119.7, 117.5, 113.9, 113.7, 68.4, 52.3; IR (neat) 3087, 3066, 3032, 2954, 1714, 1609, 1521, 1496, 1392, 1342, 1228, 1144 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}FN_2O_4$ 331.1094; Found 331.1100.

***N*-Allyl-*N*-(benzyloxycarbonyl)-4-bromo-3-methoxyaniline (5j)** (Method A): oil (0.237 g, 48%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 1H) 7.26 – 7.38 (m, 5H), 6.79 (br s, 1H), 6.72 (d, J = 8.4 Hz, 1H), 5.85 – 5.95 (m, 1H), 5.12 - 5.17 (m, 4H), 4.26 (d, J = 4.5 Hz, 2H), 3.78 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 155.9, 154.9, 136.3, 133.6, 133.0, 128.5, 128.1, 127.9, 119.6, 117.4, 111.1, 109.2, 67.5, 56.2, 53.3; IR (neat) 3087, 3067, 3032, 3008, 2939, 1706, 1587, 1488, 1449, 1392, 1244, 1211, 1145, 1056, 1024 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}BrNO_3$ 376.0549; Found, 376.0557.

***N*-Allyl-*N*-(benzyloxycarbonyl)-3-trifluoromethyl-4-methoxyaniline (5k)** (Method A): oil (0.280 g, 69%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 - 7.43 (m, 7H), 6.94 (d, J = 8.9 Hz, 1H) 5.83 - 5.91 (m, 1H), 5.10 - 5.19 (m, 4H), 4.23 (d, J = 5.8 Hz, 2H), 3.38 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 155.9, 155.2, 136.3, 133.3, 131.8, 128.4, 128.0, 127.7, 124.4, 122.1, 120.0, 119.3, 119.1, 118.8, 118.5, 117.8, 112.3, 105.0, 67.5, 56.1, 53.4; IR (neat) 3087, 3067, 3036, 3012, 2956, 2936, 2845, 1708, 1621, 1589, 1508, 1435, 1322, 1279, 1259, 1134, 1057 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{19}F_3NO_3$ 366.1317; Found 366.1324.

***N*-Allyl-*N*-(benzyloxycarbonyl)-3,4-dimethoxyaniline (5l)** (Method B): oil (0.473 g, 96%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 - 7.39 (m, 5H), 6.72 -7.82 (m, 3H), 5.87 - 5.97 (m, 1H), 5.12 - 5.19 (m, 4H),

4.24 (d, J = 5.9 Hz, 2H), 3.86 (s, 3H), 3.80 (s,3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 155.4, 148.8, 147.6, 136.7, 133.8, 128.4, 127.9, 127.6, 119.0, 117.3, 118.8, 67.2, 55.9, 55.8, 53.7; IR (neat) 3063, 3032, 3000, 2956, 2935, 2834, 1702, 1594, 1514, 1451, 1399, 1261, 1234, 1135, 1027 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}NO_4$ 328.1549; Found 328.1555.

***N*-Allyl-*N*-(benzyloxycarbonyl)-3-fluoro-4-(4-morpholinyl)aniline (5m)** (Method A): gum (1.382 g, 95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (br s, 5H), 6.95 (br s 2H), 6.86 (t, J = 9.1 Hz, 1H), 5.84 - 5.92 (m, 1H), 5.16 (br s, 3H), 5.12 (d, J = 7.8 Hz, 1H), 4.23 (d, J = 5.5 Hz, 2H), 3.87 (s, 4H) 3.08 (s,4H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 155.9, 155.2, 154.0, 138.4, 136.4, 133.4, 128.4, 128.0, 127.7,118.2, 117.4, 67.4, 67.0, 53.3, 50.9; IR (neat) 3034, 3068, 2960, 2895, 2856, 2828, 1708, 1573, 1514, 1449, 1398, 1301, 1253, 1119, 1052, 923 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{24}FN_2O_3$ 371.1771; Found 371.1779.

***N*-Allyl-*N*-(benzyloxycarbonyl)-2-aminopyridine (5n)** (Method A): oil (0.561 g, 95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 4.7 Hz, 1H), 7.59 – 7.68 (m, 2H), 7.29 - 7.35 (m, 5H), 6.99 – 7.02 (m, 1H), 5.94 (tdd, J = 5.4, 10.5, 17.0 Hz, 1H), 5.22 (s, 2H), 5.05 – 5.15 (m, 2H), 4.63 (d, J = 5.4Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ154.9, 153.8, 147.7, 137.2, 136.1, 134.1, 128.4, 128.1, 127.9, 119.9, 119.4, 116.3, 67.6, 49.1; IR (neat) 3067, 3032, 2954, 2927, 2857, 1714, 1646, 1587, 1466, 1395, 1362, 1303, 1232, 1147, 1062, 1033, 993, 920, 782 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}N_2O_2$ 269.1290; Found 269.1288.

***N*-Allyl-*N*-(benzyloxycarbonyl)-3-aminopyridine (5o)** (Method A): oil (0.441 g, 75%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.44 (d, J = 3.4 Hz, 1H), 7.21 - 7.32 (m, 1H), 7.21 - 7.32 (m, 6H), 5.84 - 5.94 (m, 1H), 5.12 - 5.17 (m, 4H), 4.29 (d, J = 5.5 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.8, 147.8, 147.2, 138.5, 136.0, 133.8, 133.0, 128.4, 128.1, 127.8, 123.4, 117.7, 67.7, 53.0; IR (neat) 3036,

2954, 1709, 1581, 1482, 1430, 1306, 1361, 1234, 1148, 1957, 1016, 926, 812 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{16}N_2O_2Na$ 291.1110; Found 291.1100.

***N*-Allyl-*N*-(benzyloxycarbonyl)-4-aminopyridine (5p)** (Method A): oil (0.416 g, 71%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 2H), 7.24 – 7.33 (m, 7H), 5.83 – 5.93 (m, 1H), 5.10 - 5.21 (m, 4H), 4.34 (, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.2. 150.3, 149.4, 135.7, 133.0, 128.5, 128.3, 128.0, 118.3, 117.0, 68.0, 51.6; IR (neat) 3033, 2956, 1713, 1590, 1563, 1500, 1451, 1392, 1364, 1285, 1149, 1034, 994, 924, 826 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}N_2O_2$ 269.1290; Found 269.1281.

***N*-Allyl-*N*-(benzyloxycarbonyl)-2-aminoquinoline (5q)** (Method A): oil (0.212 g, 91%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 9.0 Hz, 1H), 7.89 (d, J = 8.5 Hz, 1H), 7.82 (d, J = 8.9 Hz, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.39-7.29 (m, 5H), 6.01 (ddt, J = 5.6, 11.2, 16.3 Hz, 1H), 5.25 (s, 2H), 5.18 (d, J = 17.1 Hz, 1H), 5.08 (d, J = 10.2 Hz, 1H), 4.80 (d, J = 8 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.1, 153.1, 146.5, 136.9, 136.0, 134.2, 129.4, 128.5, 128.4, 128.2, 128.0, 127.2, 125.9, 125.6, 118.6, 116.6, 67.8, 49.3. IR (neat): 3066, 2955, 1712, 1601, 1502, 1394, 1363, 1329, 1286, 1230, 1145, 1046, 919, 826 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{18}N_2O_2Na$ 341.1266; Found 341.1265.

***N*-Allyl-*N*-(benzyloxycarbonyl)-3-aminoquinoline (5r)** (Method A): oil (0.418 g, 90%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (br s, 1H), 8.07 (d, J = 8.5 Hz, 1H), 7.95 (br s, 1H), 7.73 (d, J = 8.2 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.24 - 7.31 (m, 5H), 5.93 (ddt, J = 5.8, 11.5, 15.9 Hz, 1H), 5.13 – 5.18 (m, 4H), 4.37 (d, J = 5.8, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.0, 150.0, 146.1, 136.0, 135.5, 133.1, 131.3, 129.3, 129.2, 128.4, 128.2, 127.9, 127.8, 127.7, 127.1, 117.9, 67.8, 53.3. IR (neat): 3064, 3034, 1713, 1606, 1496, 1452, 1402, 1365, 1327, 1289, 1246, 1147, 1038, 966, 922, 786 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{18}N_2O_2Na$ 341.1266; Found 341.1263.

***N*-Allyl-*N*-(benzyloxycarbonyl)-6-aminoquinoline (5s)** (Method A): oil (0.437 g, 94%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (br s, 1H), 8.05 (d, J = 8.5 Hz, 2H), 7.64 (s, 1H), 7.59 (d, J = 8.3 Hz, 1H), 7.33 (dd, J = 4.1, 8.0 Hz, 1H), 7.27 (s, 5H), 5.93 (ddt, J = 5.7, 10.6, 16.1 Hz, 1H), 5.20 (s, 2H), 5.14 (d, J = 9.7 Hz, 2H), 4.36 (d, J = 5.6 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.1, 150.4, 146.6, 140.1, 136.3, 135.8, 133.5, 130.0, 129.1, 128.5, 128.4, 128.2, 128.0, 127.8, 123.9, 121.4, 117.4, 67.6, 53.3; IR (neat): 3066, 2952, 1707, 1596, 1501, 1448, 1400, 1358, 1319, 1283, 1231, 1029, 991, 923, 838, 768 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{18}N_2O_2Na$ 341.1266; Found 341.1253.

***N*-Allyl-*N*-(benzyloxycarbonyl)-8-aminoquinoline (5t)** (Method A): oil (0.408 g, 87%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.12 (d, J = 8.2 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.56 (br s, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.34 - 7.38 (m, 1H), 7.17 (br s, 4H), 6.96 (br s, 1H), 5.92 - 6.01 (m, 1H), 5.01 - 6.01 (m, 4H), 4.76 (br s, 1H), 4.18 (br s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 156.3, 150.3, 144.5, 139.1, 136.7, 136.1, 134.2, 129.3, 128.1, 127.6, 127.5,127.3, 126.1, 121.4, 117.2, 67.1, 53.6; IR (neat): 3065, 2948, 1701, 1614, 1597, 1499, 1446, 1400, 1356, 1284, 1237, 1147, 1102, 985, 924, 835, 798, 761 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{18}N_2O_2Na$ 341.1266; Found 341.1262.

Procedure for the Synthesis of *N*-Allyl Carbamates 8 and 9. To the 2-aminothiazole-derived carbamate **7** (1.25 g, 5.34 mmol) in 50 mL of dry THF was added 60% NaH (0.256 g, 6.41mmol), allyl bromide (0.712 g, 5.87mmol), and tetrabutylammonium iodide (0.237 g, 0.641 mmol). After stirring overnight at 25 °C under argon, H_2O (1 mL) was added dropwise followed by the addition of CH_2Cl_2 (100 mL). The mixture was washed with H_2O (2 x 50 mL) and dried over $CaCl_2$. Removal of the solvent by rotary evaporation under reduced pressure afforded a viscous liquid that was chromatographed on silica gel, eluting first with 1:1:1 hexanes-EtOAc-CH_2Cl_2 and then 1:3 EtOAc-CH_2Cl_2 to give, after combining appropriate fractions and concentration under reduced pressure, **8** as a viscous oil (1.05 g, 72%) and **9** as an off-white solid (0.35 g, 25%).

***N*-Allyl-*N*-(benzyloxycarbonyl)-2-aminothiazole (8)**: oil (1.05 g, 72%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.42 (m, 6H), 6.94 (s, 1H), 5.89 – 6.00 (m, 1H), 5.31 (s, 2H), 5.17 (d, J = 10 Hz, 1H), 5.13 (s, 1H), 4.90 (d, J = 4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.2, 154.1, 137.8, 135.4, 132.4, 128.8, 128.6, 128.3, 117.2, 114.7, 68.7, 49.2; IR (neat): 1631, 1467,1412, 1359,1142, 1086, 868,825, 776, 715, 471 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O_2S$, 275.0854; Found 275.0860.

***N*-[3-(propen-3-yl)-2(3H)-thiazolylidene]carbamic acid, benzyl ester (9)**: off-white solid: mp 72-73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 - 7.42 (m, 5H), 6.81 (d, J = 4.7 Hz, 1H), 6.54 (d, J = 4.7 Hz, 1H), 5.83 – 5.93 (m, 1H), 5.23 (d, J = 9.4 Hz, 1H), 5.21 (s, 2H), 5.14 (d, J = 17.1 Hz, 1H), 4.65 (br d, J = 5.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.3, 163.0, 141.2, 137.0, 131.5, 128.6, 128.5, 128.0, 127.5, 127.0, 125.9, 119.3, 108.2, 67.6, 66.2, 50.3; IR (neat): 3083, 1564, 1450, 1412, 1359, 1336, 1212, 1110, 1086, 1069, 987, 945, 904, 825, 776, 716, 621, 553 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O_2S$ 275.0854; Found 275.0863.

General Procedure for the Iodocyclocarbamation Reaction of *N*-Allylated *N*-Arylcarbamates 5a-m to give 5-(iodomethyl)oxazolidinones 6a-m. To a solution of the *N*-allylated *N*-arylcarbamate (1.64 mmol) in CH_2Cl_2 (25 mL) under N_2 was added I_2 (0.831 g, 3.27 mmol). The dark brown solution was then stirred at ambient temperature under N_2 and reaction progress monitored by TLC (hexane/EtOAc). When the reaction was complete the mixture was diluted with CH_2Cl_2, poured into 10% aqueous $Na_2S_2O_3$, and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude product. Chromatography over silica gel, eluting with hexane/EtOAc, afforded, after combining appropriate fractions and concentration under reduced pressure, generally high yields of the targeted 5-(iodomethyl)oxazolidinone products.

(±)-(3-Phenyl-2-oxo-5-oxazolidinyl)methyl iodide (6a): solid (20.858 g, 97%): mp 97-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 7.9 Hz, 2H), 7.39 (t, J = 7.9 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 4.70 – 4.77 (m, 1H), 4.18 (t, J = 8.9 Hz, 1H), 3.79 (dd, J = 7.1, 9.2 Hz, 1H), 3.47 (dd, J = 4.2, 10.3 Hz, 1H), 3.35 (dd, J = 7.4, 10.3 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 155.0, 137.8, 129.2, 124.4, 118.4, 71.3, 51.1, 6.0; IR (neat): 3036, 2956, 2889, 1748, 1598, 1503, 1481, 1407, 1306, 1226, 1129, 977, 755 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}INO_2$ 303.9835; Found 303.9840.

(±)-[3-(2-Methylphenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6b): gum (0.195 g, 70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 4H), 4.71 – 4.76 (m, 1H), 4.06 (t, J = 8.9 Hz, 1H), 3.69 (dd, J = 6.2, 9.1 Hz, 1H), 3.40 – 3.50 (m, 2H), 2.32 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.4, 135.9, 135.5, 131.4, 128.4, 127.1, 126.6, 72.0, 53.5, 18.0, 6.6; IR (neat): 3024, 2952, 2921, 2853, 1754, 1495, 1410, 1238, 1142, 1011, 977, 755 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{13}INO_2$ 317.9991; Found 317.9999.

(±)-[3-(2,6-Dimethylphenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6c): gum (0.170 g, 86%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 – 7.17 (m, 3H), 4.72 - 4.79 (m, 1H), 3.88 (t, J = 9.4 Hz, 1H), 3.55 – 3.60 (m, 1H), 3.45 – 3.49 (m, 1H), 3.46 – 3.41 (m, 1H), 2.28 (s, 3H), 2.25 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.4, 136.7, 136.6, 133.5, 128.9, 128.8, 128.7, 72.4, 51.8, 18.1, 17.7, 6.4; IR (neat): 3024, 2956, 2921, 2857, 1747, 1529, 1484, 1408, 1250, 1236, 1132, 1086, 976, 775, 758 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{15}INO_2$ 332.0147; Found 332.0156.

(±)-[3-(4-Bromophenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6d): solid (0.720 g, 95%): mp 152-154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.7 Hz, 2H), 7.44 (d, J = 9.0 Hz, 2H), 4.70 - 4.77 (m, 1H), 4.15 (t, J = 8.9 Hz, 1H), 3.76 (dd, J = 6.2, 9.1 Hz, 1H), 3.46 – 3.50 (m, 1H), 3.33 – 3.38 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.8, 136.9, 132.1, 120.0, 117.2, 71.2, 50.9, 5.9; IR (ATR) 3118,

3068, 3022, 2960, 2922, 2852, 1735, 1589, 1492, 1395, 1359, 1300, 1214, 1193, 1132, 1077, 982, 824, 749 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_{10}BrINO_2$ 381.8940; Found 381.8943.

(±)-[3-(4-Iodophenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6e): solid (0.274 g, 94%): mp 145-148 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 9.0 Hz, 2H), 7.62 (d, J = 9.0 Hz, 2H), 4.70 - 4.76 (m, 1H), 4.14 (t, J = 8.9 Hz, 1H), 3.73 – 3.77 (m, 1H), 3.45 – 3.49 (m, 1H), 3.33 – 3.38 (m, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 153.7, 138.0, 137.6, 120.1, 87.8, 71.2, 50.8, 6.0; IR (neat): 3095, 3024, 2956, 2920, 2892, 2853, 1754, 1586, 1489, 1417, 1396, 1306, 1223, 1132, 979, 821, 748 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_{10}I_2NO_2$ 429.8801; Found 429.8816.

(±)-[3-(3,4,5-Trifluorophenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6f): solid (0.248 g, 89%): mp 67.5-69.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22 (dd, J = 5.9, 9.6 Hz, 2H), 7.62, 4.67 - 4.74 (m, 1H), 4.09 (t, J = 8.9 Hz, 1H), 3.69 (dd, J = 6.1, 9.1 Hz, 1H), 3.42 – 3.46 (m, 1H), 3.33 – 3.37 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.4, 152.6, 152.5, 152.4, 152.4, 150.1, 150.0, 149.9, 149.9, 137.8, 137.6, 137.5, 135.3, 135.2, 135.0, 133.6, 133.5, 133.4, 133.4, 133.3, 102.8, 102.7, 102.6, 102.5, 71.1, 50.8, 6.7; IR (neat): 3109, 2956, 2893, 1756, 1622, 1530, 1456, 1426, 1255, 1117, 1046, 830, 777, 750, 710 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_8F_3INO_2$ 357.9552; Found 357.9561.

(±)-[3-(2,3,4-Trifluorophenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6g): solid (0.546 g, 92%): mp 89-90 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.29 (m, 1H), 6.97- 7.04 (m, 1H), 4.71- 4.77 (m, 1H), 4.16 (t, J = 8.8 Hz, 1H), 3.74 (dd, J = 7.1, 10.1 Hz, 1H), 3.38 – 3.47 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.0, 151.2, 151.2, 151.1, 151.0, 148.7, 148.7, 148.6, 148.6, 148.1, 148.0, 148.0, 147.9, 145.6, 145.5, 145.4, 145.4, 141.9, 141.7, 141.7, 141.6, 139.4, 139.2, 139.2, 139.1, 122.5, 122.5, 122.4, 122.4, 121.1, 121.1, 121.1, 121.0, 121.0, 121.0, 112.2, 112.1, 112.0, 112.0, 72.3, 52.4, 52.3, 6.1; IR (neat): 3097, 3028, 2960, 2914, 2849, 1760, 1617, 1517, 1410, 1287, 1233, 1133, 1014, 810, 753, 704 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_8F_3INO_2$ 357.9552; Found 357.9563.

(±)-[3-[3,5-bis(trifluoromethyl)phenyl]-2-oxo-5-oxazolidinyl]methyl iodide (6h): solid (0.085 g, 78%): mp 104.5-105.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 2H), 7.63 (s, 1H), 4.74 – 4.81 (m, 1H), 4.28 (t, J = 8.8 Hz, 1H), 3.87 (dd, J = 6.1, 8.9 Hz, 1H), 3.50 – 3.54 (m, 1H), 3.41 – 3.45 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 153.5, 139.3, 133.0, 132.7, 132.4, 132.2, 126.2, 124.1, 121.9, 119.7, 117.5, 117.5, 117.4, 117.4, 71.4, 50.7, 5.6; IR (neat): 3115, 3079, 2960, 2897, 1759, 1623, 1477, 1409, 1278, 1183, 1133, 879, 751 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_9F_6INO_2$ 439.9582; Found 439.9593.

(±)-[3-(3-fluoro-4-nitrophenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6i): gum (0.105g, 74%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (t, J = 8.8 Hz, 1H), 7.71 (d, J = 13.2 Hz, 1H), 7.39 (d, J = 9.5, 1H), 4.78 - 4.85 (m, 1H), 4.25 (t, J = 9.0 Hz, 1H), 3.85 (dd, J = 5.9, 9.1, 1H), 3.50 – 3.54 (m, 1H), 3.39 – 3.44 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 157.5, 155.4, 153.1, 144.2, 144.1, 132.5, 127.4, 112.6, 107.2, 107.0, 71.3, 50.7, 5.7; IR (neat): 3119, 3067, 2956, 2920, 2849, 1759, 1610, 1518, 1402, 1339, 1214, 1130, 1017, 836, 747 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_9FIN_2O_4$ 366.9591; Found 366.9597.

(±)-[3-(4-bromo-3-methoxyphenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6j): solid (0.118 g, 70%): mp 111-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.49 (d, J = 8.6 Hz, 1H), 6.67 (d, J = 8.6 Hz, 1H), 4.70 - 4.76 (m, 1H), 4.16 (t, J = 8.9 Hz, 1H), 3.92 (s, 3H), 3.75 – 3.79 (m, 1H), 3.46 – 3.50 (m, 1H), 3.34 – 3.39 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 156.3, 153.8, 138.4, 133.1, 110.6, 106.6, 103.0, 71.1, 56.4, 51.0, 6.0; IR (neat): 3119, 3008, 2960, 2926, 2849, 1749, 1593, 1494, 1405, 1233, 1128, 1053, 742 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{12}BrINO_3$ 411.9046; Found 411.9056.

(±)-[3-(3-trifluoromethyl-4-methoxyphenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6k): solid (0.155 g, 73%): mp 134-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 9.6 Hz, 1H), 7.62 (s, 1H), 7.03 (d, J = 9.2 Hz, 1H), 4.71 - 4.77 (m, 1H), 4.17 (t, J = 9.1 Hz, 1H), 3.91 (s, 3H), 3.77 (dd, J = 6.3, 8.8 Hz, 1H),

3.46 – 3.50 (m, 1H), 3.36 – 3.41 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 154.1, 130.5, 124.3, 123.9, 122.1, 119.4, 119.2, 118.9, 118.7, 117.8, 117.7, 117.7, 117.6, 112.9, 71.2. 56.3, 51.3. 6.0; IR (neat): 3111, 3012, 2960, 2924, 2850, 1752, 1591, 1509, 1440, 1331, 1267, 1226, 1127, 1057, 819, 748 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{12}F_3INO_3$ 401.9814; Found 401.9825.

(±)-[3-(3,4-dimethoxyphenyl)-2-oxo-5-oxazolidinyl]methyl iodide (6l): solid (0.210 g, 94%): mp 189-190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 6.81 (d, J = 8.7 Hz, 1H), 6.71 (dd, J = 2.6, 8.7 Hz, 1H), 4.64 - 4.72 (m, 1H), 4.12 (t, J = 8.9 Hz, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.73 (dd, J = 6.1, 9.2 Hz, 1H), 3.44 (dd, J = 3.9, 10.3 Hz, 1H), 3.32 (dd, J = 8.4, 10.3 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.2, 149.3, 146.1, 131.4, 111.1, 110.2, 103.8, 71.1, 56.1, 56.0, 51.5, 6.1; IR (ATR): 3024, 2958, 2934, 2849, 1724, 1608, 1590, 1514, 1452, 1241, 1215, 1128, 1083, 1012, 830, 818, 748 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{15}INO_4$ 364.0046; Found 364.0056.

(±)-[3-[3-fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl iodide (6m): white solid (0.563 g, 85%): mp 145.5-146.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, J = 2.6, 14.1 Hz, 1H), 7.13 (d, J = 8.6 Hz, 1H), 6.94 (t, J = 9.0 Hz, 1H), 4.69 – 4.76 (m, 1H), 4.14 (t, J = 8.9 Hz, 1H), 3.87 (t, J = 4.5 Hz, 4H), 3.74 (dd, J = 6.8, 8.8 Hz, 1H), 3.47 (dd, J = 3.4, 10.3 Hz, 1H), 3.36 (t, J = 9.5 Hz, 1H), 3.06 (t, J = 4.6 Hz, 4H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 156.7, 154.2, 153.8, 136.6, 136.5, 132.8, 132.7, 118.8, 118.7, 114.0, 113.9, 107.7, 107.4, 71.1, 66.9, 51.1, 51.0, 50.9, 6.1; IR (ATR): 3091, 3020, 3000, 2963, 2951, 2923, 2891, 2853, 2838, 1733, 1628, 1571, 1515, 1420, 1226, 1191, 1170, 1116, 1095, 818, 808, 746 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{17}FIN_2O_3$ 407.0268; Found 407.0278.

General Procedure for the Iodocyclocarbamation Reaction of *N*-Allylated *N*-Heteroarylcarbamates 5o-p, **r-s to give 5-(iodomethyl)oxazolidinones 6o-p**, **r-s.** To a solution of the *N*-allylated *N*-heteroarylcarbamate (0.48 mmol) in CH_3CN (8 mL) was added pyridine (0.389 mL, 4.84 mmol) and I_2 (0.369 g, 1.45 mmol). The resulting solution was then heated to 81 °C under Ar, typically

for 24 h. After cooling to ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with 10% aqueous $Na_2S_2O_3$ (7.5 mL) and then H_2O (7.5 mL). After drying over $CaCl_2$, the solvent was removed under reduced pressure to give a crude product. Chromatography of the residue over silica gel, eluting with CH_2Cl_2/EtOAc (sometimes with 2-4% MeOH added) provided, after combining appropriate fractions and concentration under reduced pressure, variable yields of the targeted 5-(iodomethyl)oxazolidinone products.

(±)-[3-(3-pyridinyl)-2-oxo-5-oxazolidinyl]methyl iodide (6o): To a solution of *N*-allylcarbamate **5o** (0.130 g, 0.484 mmol) in CH_3CN (8 mL) was added I_2 (0.369 g, 1.45 mmol) and pyridine (0.383 g, 0.389 mL, 4.84 mmol). The resulting solution was heated to 81° under Ar for 24 h. After cooling, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with 10% aqueous $Na_2S_2O_3$ (10 mL) and then H_2O (10 mL). After drying the organic layer over $CaCl_2$, the solvent was removed on a rotary evaporator under reduced pressure. Chromatography of the residue on silica gel, eluting with CH_2Cl_2/EtOAc (4:1, 1:1 and then 1:2) afforded 0.006 g (5%) of recovered **5o** (3%) followed by 0.084 g (57%) of the title compound as a solid: mp 84-85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, J = 2.7 Hz, 1H), 8.40 (d, J = 4.6 Hz, 1H), 8.10 – 8.13 (m, 1H), 7.32 (dd, J = 4.6, 8.5 Hz, 1H), 4.75 – 4.81 (m, 1H), 4.23 (t, J = 8.0 Hz, 1H), 3.82 (dd, J = 6.1, 9.1 Hz, 1H), 3.49 (dd, J = 4.0, 10.5 Hz, 1H), 3.42 (dd, J = 7.7, 10.5 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.9, 145.4, 139.2, 134.5, 125.5, 123.6, 71.5, 50.2, 6.2; IR (ATR): 3041, 2959, 1751, 1579, 1486, 1439, 1406, 1365, 1314, 1230, 1190, 1134, 1090, 1016, 980, 805 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_9H_9IN_2O_2Na$ 326.9607; Found 326.9593.

(±)-[3-(4-pyridinyl)-2-oxo-5-oxazolidinyl]methyl iodide (6p): To a solution of *N*-allylcarbamate **5p** (0.130 g, 0.484 mmol) in CH_3CN (8 mL) was added I_2 (0.369 g, 1.45 mmol) and pyridine (0.383 g, 0.389 mL, 4.84 mmol). The resulting solution was heated to 81° under Ar for 24 h. After cooling, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with 10% aqueous $Na_2S_2O_3$ (10 mL) and

then H_2O (10 mL). After drying the organic layer over $CaCl_2$, the solvent was removed on a rotary evaporator under reduced pressure. Chromatography of the residue on silica gel, eluting with EtOAc/CH_2Cl_2/CH_3OH (20:77:3 and then 20:76:4) afforded 0.012 g (9%) of recovered **5p** and 0.056 g (38%) of the desired product as a yellow solid. An analytical sample was obtained by recrystallization from toluene/ethyl acetate to give yellow crystals with the following characteristics: mp 118-119 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 2H), 7.50 (s, 2H), 4.79 (br s, 1H), 4.16 - 4.24 (m, 1H), 3.76 - 3.83 (m, 1H), 3.37 - 3.54 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.3, 149.6, 143.6, 110.8, 70.5, 48.9, 4.9. IR (neat): 3033, 1759, 1594, 1506, 1404, 1321, 1218, 1136, 989, 820 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_9H_{10}IN_2O_2$ 304.9787; Found 304.9781.

(±)-[3-(3-quinolinyl)-2-oxo-5-oxazolidinyl]methyl iodide (6r): To a solution of *N*-allylcarbamate **5r** (0.077 g, 0.242 mmol) in CH_3CN (5 mL) was added I_2 (0.185 g, 0.725 mmol) and pyridine (0.192 g, 0.198 mL, 2.42 mmol). The resulting solution was heated to 80^o under Ar for 24 h. After cooling, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with 10% aqueous $Na_2S_2O_3$ (5 mL) and then H_2O (5 mL). After drying the organic layer over $CaCl_2$, the solvent was removed on a rotary evaporator under reduced pressure and the residue chromatographed over silica gel, eluting with CH_2Cl_2/EtOAc (1:1) to give 0.0545 g (64%) of the title compound as an off-white solid: mp 166-168 ^oC (dec); ^1H NMR (400 MHz, $CDCl_3$) δ 9.11 (d, J = 2.7 Hz, 1H), 8.21 (d, J = 2.7 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 7.4 Hz, 1H), 7.60 (ddd, J = 1.4, 6.9, 8.3 Hz, 1H), 7.49 (ddd, J = 1.1, 6.9, 9.1 Hz, 1H), 4.76 (ddt, J = 3.9, 6.1, 8.3 Hz, 1H), 4.25 (t, J = 8.8 Hz, 1H), 3.87 (dd, J = 6.1, 9.1 Hz, 1H), 3.46 (dd, J = 3.9, 10.5 Hz, 1H), 3.36 (dd, J = 8.1, 10.5 Hz, 1H), $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.0, 145.0, 142.2, 131.5, 129.1, 128.7, 127.6, 127.5, 127.4, 122.7, 71.7, 50.6, 5.86. IR (neat): 3011, 2950, 1737, 1602, 1491, 1410, 1377, 1240, 1190, 1142, 1097, 1021, 894, 862, 785 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{12}IN_2O_2$ 354.9944; Found 354.9935.

(±)-[3-(6-quinolinyl)-2-oxo-5-oxazolidinyl]methyl iodide (6s) To a solution of *N*-allylcarbamate **5s** (0.154 g, 0.484 mmol) in CH_3CN (8 mL) was added I_2 (0.369 g, 1.45 mmol) and pyridine (0.383 g, 0.389 mL, 4.84 mmol). The resulting solution was heated to reflux temperature under N_2 for 22 h. After cooling, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with 10% aqueous $Na_2S_2O_3$ (7.5 mL) and then H_2O (10 mL). After drying the organic layer over $CaCl_2$, the solvent was removed on a rotary evaporator under reduced pressure and the residue chromatographed over silica gel, eluting with EtOAc/CH_2Cl_2 (45:55 and then 55:45) to give, after concentration of appropriate fractions, 0.103 g (60%) of the title compound as a light yellow solid: mp 168-170 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.79, (dd, J = 1.7, 4.1 Hz, 1H), 8.32 (d, J = 8.3 Hz, 1H), 8.21 (dd, J = 2.5, 9.3 Hz, 1H), 8.01 (d, J = 9.3 Hz, 1H), 7.88 (d, J = 2.2 Hz, 1H), 7.49 (dd, J = 4.2, 8.3 Hz, 1H), 4.81-4.75 (m, 1H), 4.31 (t, J = 9.0 Hz, 1H), 3.79 (dd, J = 6.0, 9.2 Hz, 1H), 3.62 (dd, J = 5.3, 10.7 Hz, 1H), 3.57 (dd, J = 4.8, 10.8 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 154.2, 150.0, 144.9, 136.6, 136.0, 130.1, 128.5, 122.4, 121.8, 114.7, 71.5, 51.0, 9.98. IR (neat): 1745, 1622, 1502, 1405, 1361, 1290, 1223, 1111, 1006, 832 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{11}IN_2O_2Na$ 376.9763; Found 376.9766.

(±)-[3-[3-Fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl azide (10). A solution of (±)-[3-[3-fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl iodide (**6m**, 0.081 g, 0.20 mmol) in dry DMF (4 mL) under N_2 was treated with solid NaN_3 (0.052 g, 0.79 mmol, 4 equivalents) at ambient temperature. The stirred slurry was then heated to 65 °C for 2 h, at which time TLC analysis (1:1 hexane/EtOAc, short wave UV) revealed the reaction to be complete. After cooling to ambient temperature, the reaction mixture was transferred to a separatory funnel with H_2O and EtOAc. The mixture was extracted with EtOAc. The combined EtOAc extracts were thoroughly washed with H_2O and brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give 0.060 g (95%) of the title azide as an off-white solid: mp 109-110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, J = 14.3, 2.6 Hz, 1H), 7.12

(d, J = 9.0 Hz, 1H), 6.94 (t, J = 9.1 Hz, 1H), 4.79 (m, 1H), 4.05 (t, J = 9.0 Hz, 1H), 3.87 (m, 4H), 3.82 (dd, J = 8.8, 6.3 Hz, 1H), 3.70 (dd, J = 13.2, 4.5 Hz, 1H), 3.59 (dd, J = 13.2, 4.3 Hz, 1H), 3.05 (m, 4H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 156.5, 154.5, 153.8, 136.5, 132.9, 118.9, 118.8, 113.9, 113.9, 107.6, 107.4, 70.6, 66.9, 53.0, 51.0, 47.5; IR (ATR) 2963, 2922, 2901, 2879, 2852, 2831, 2096, 1742, 1629, 1573, 1518, 1416, 1364, 1218, 1196, 1111 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{17}FN_5O_3$ 322.1315; Found 322.1321.

(±)-[[3-[3-Fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (11). A solution of (±)-[3-[3-fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl azide (**10**, 0.058 g, 0.18 mmol) in dry THF (5 mL) was treated with triphenylphosphine (0.052 g, 0.20 mmol) at ambient temperature. After 4.0 h, TLC analysis (1:1 hexane/EtOAc, short wave UV) revealed that conversion to the iminophosphorane intermediate was incomplete. Additional triphenylphosphine (0.025 g, 0.10 mmol) was added and the reaction mixture stirred overnight at ambient temperature, at which time TLC analysis revealed the reaction to be complete. H_2O (0.100 mL) was added and the reaction mixture heated to 40 °C (internal temperature) for 5 h. At this point, TLC analysis (10% MeOH/CH_2Cl_2) indicated complete hydrolysis of the iminophosphorane intermediate to the corresponding 5-(aminomethyl)oxazolidinone intermediate. The reaction mixture was first concentrated by rotary evaporation (benzene was added several times to azeotrope off the H_2O) and then under high vacuum to give the crude amine as a pale-yellow gum. This material was dissolved in CH_2Cl_2 (4 mL), treated with pyridine (0.143 g, 0.145 mL, 1.80 mmol) and acetic anhydride (0.092 g, 0.085 mL, 0.90 mmol), and then stirred overnight at ambient temperature. TLC analysis (10% MeOH/CH_2Cl_2) showed complete conversion of the amine to the corresponding acetamide. The reaction mixture was concentrated *in vacuo* to a pale-yellow solid which was purified by column chromatography over silica gel (packed with CH_2Cl_2, eluting with 20-60% acetone/CH_2Cl_2) to give, after concentration of appropriate fractions,

0.051 g (83%) of the title compound as a white solid: mp 184.5-185.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, J = 14.4, 2.4 Hz, 1H), 7.07 (d, J = 8.8 Hz, 1H), 6.91 (t, J = 9.1 Hz, 1H), 6.68 (t, J = 5.8 Hz, 1H), 4.78 (m, 1H), 4.02 (t, J = 9.0 Hz, 1H), 3.87 (m, 4H), 3.77 (dd, J = 8.9, 6.9 Hz, 1H), 3.65 (t, J = 5.0 Hz, 2H), 3.05 (m, 4H), 2.02 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.3, 156.6, 154.4, 154.2, 136.5, 136.5, 132.9, 132.8, 118.8, 118.7, 113.9, 113.9, 107.6, 107.4, 105.0, 72.0, 66.9, 50.9, 50.9, 47.6, 41.8, 23.0; IR (ATR) 3338, 3117, 3076, 2970, 2926, 2864, 2816, 1733, 1659, 1546, 1515, 1425, 1228, 1115 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{21}FN_3O_4$ 338.1516; Found 338.1524.

Pyridinium salt 12: To a solution of *N*-allylcarbamate **5n** (0.065 g, 0.242 mmol) in CH_2Cl_2 (4 mL) was added I_2 (0.123 g, 0.484 mmol) and the resulting solution was stirred at ambient temperature for 1.5 h. TLC analysis (silica gel, 2:20:78 methanol/EtOAc/CH_2Cl_2) revealed that **5n** was consumed and a new product of much lower R_f had formed. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and washed with 10% aqueous $Na_2S_2O_3$ (5 mL), followed by an aqueous solution of KI (0.5 g in 5 mL H_2O). Without drying (a solid forms when the solution is dried over $CaCl_2$), the bulk of the CH_2Cl_2 was removed on a rotary evaporator under reduced pressure. The solid residue was recrystallized from toluene/methanol to give 0.101 g (69%) of **12** as white crystals: mp = 137-8 °C (dec with the evolution of a gas); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.89 (d, J = 6.3 Hz, 1H), 8.50 (t, J = 8.1 Hz, 1H), 8.15 (d, J = 8.7 Hz, 1H), 7.68 (t, J = 6.9 Hz, 1H), 7.47-7.32 (m, 3H), 7.22-7.09 (m, 2H), 5.45-5.36 (m, 1H), 5.36 (s, 2H), 4.48 (t, J = 10.6 Hz, 1H), 3.98 (dd, J = 5.6, 10.9 Hz, 1H), 3.97, 3.90 (d, J = 4.1 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 150.6, 148.6, 138.8, 135.3, 129.3, 129.1, 128.7, 125.7, 120.8, 114.1, 69.3, 62.44, 51.65, 9.57; IR (neat) 2916, 1736, 1627, 1509, 1412, 1255 cm^{-1}; HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{16}H_{16}IN_2O_2$ 395.0257; Found 395.0262.

Quinolinium salt 13: To a solution of *N*-allylcarbamate **5q** (0.065 g, 0.204 mmol) in $CHCl_3$ (5 mL) was added I_2 (0.104 g, 0.408 mmol) and the solution stirred under Ar at ambient temperature for 1.5 h. The

reaction mixture was diluted with CH_2Cl_2 (5 mL) and washed with 10% aqueous $Na_2S_2O_3$ (5 mL), followed by an aqueous solution of KI (0.5 g in 5 mL H_2O). After drying over the organic layer over $CaCl_2$, the bulk of the solvent was removed in a rotary evaporator under reduced pressure. The solid residue was recrystallized from toluene/methanol to give 0.0839 g (72%) of **13** as a light yellow crystalline solid: mp 145-150 ^oC (dec); ^1H NMR (400 MHz, DMSO-d_6) δ 9.10 (d, J = 9.5 Hz, 1H), 8.33 (d, J = 7.9 Hz, 2H), 8.24 (d, J = 8.6 Hz, 1H), 8.12 (t, J = 7.9 Hz, 1H), 7.84 (6, J = 7.1 Hz, 1H), 7.51-7.36 (m, 5H), 5.95-5.90 (m, 1H), 5.43 (s, 2H), 4.58 (t, J = 10.6 Hz, 1H), 4.28 (d, J = 11.2 Hz, 1H), 3.96-3.91 (m, 1H), 3.84 (d, J = 11.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 151.6, 150.5, 149.7, 136.0, 135.1, 134.2, 131.1, 129.2, 129.1, 128.7, 128.4, 125.1, 117.5, 111.5, 69.7, 59.6, 52.5, 8.9; IR (solid film): 2920, 1741, 1600, 1533, 1385, 1301, 1266, 1221, 1144, 1071, 827 cm^{-1}; HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{20}H_{18}IN_2O_2$ 445.0413; Found 445.0414.

Quinolinium salt 14: To a solution of *N*-allylcarbamate **5t** (0.065 g, 0.204 mmol) in $CHCl_3$ (5 mL) was added I_2 (0.104 g, 0.408 mmol) and the solution stirred under Ar at ambient temperature for 1.5 h. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and washed with 10% aqueous $Na_2S_2O_3$ (5 mL), followed by an aqueous solution of NaI (0.5 g in 5 mL H_2O). After drying over the organic layer over $CaCl_2$, the bulk of the solvent was removed in a rotary evaporator under reduced pressure. The solid residue was recrystallized from toluene/methanol to give 0.102 g (87%) of **14** as a light yellow crystalline solid: mp 155-157 ^oC (dec). ^1H NMR (400 MHz, DMSO-d_6) δ 9.58 (d, J = 5.6 Hz, 1H), 9.34 (d, J = 8.1 Hz, 1H), 8.61 (d, J = 8.0 Hz, 1H), 8.25 (dd, J = 5.8, 8.4 Hz, 1H), 8.21 (d, J = 8.2 Hz, 1H), 8.00 (t, J = 8.1 Hz, 1H), 7.49 (d, J = 6.3 Hz, 2H), 7.33-7.40 (m, 3H), 5.51 (t, J = 7.0 Hz, 1H), 5.33 (AB q, J = 12 Hz, 2H), 5.09 (d, J = 14 Hz, 1H), 4.06 (dd, J = 2.6, 14.3 Hz, 1H), 3.57-3.65 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 149.3, 145.5, 144.8, 132.1, 126.4, 126.3, 125.7, 125.1, 124.9, 124.8,

124.0, 123.2, 121.9, 118.4, 64.9, 60.9, 40.3, 0.0; IR (neat): 1711, 1530, 1423, 1242 cm^{-1}; HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{20}H_{18}IN_2O_2$ 445.0413; Found 445.0414.

***N*-1,3-pentadien-5-yl *N*-Phenylcarbamate (18).** To a solution of benzyl *N*-phenylcarbamate (0.512 g, 2.25 mmol) in dry DMF (25 mL) under N_2 was added Cs_2CO_3 (2.223 g, 6.75 mmol), *n*-Bu_4NI (1.660 g, 4.50 mmol) and then 5-bromo-1,3-pentadiene[20] (0.669 g, 4.50 mmol). The resultant mixture was warmed to 40 °C and stirred under N_2 until TLC analysis (3:1 hexane/EtOAc) revealed the reaction to be complete. The reaction mixture was cooled to ambient temperature, treated with H_2O (54 mL), and then extracted with 1:1 hexane/Et_2O (3 x 200 mL). The combined organic extracts were washed once with H_2O and brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product. Chromatography over silica gel, eluting with 3:1 hexane/EtOAc, afforded, after combining appropriate fractions and concentration under reduced pressure, 0.531 g (80%) of the title compound as a pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.35 (m, 10 H), 6.25 – 6.32 (m, 1H), 6.10 (dd, J = 10.4, 15.3 Hz, 1H), 5.77 (dt, J = 12.3, 7.5 Hz, 1H), 5.16 (s, 2H), 5.13 (d, J = 16.5 Hz, 1H), 5.05 (d, J = 10.2 Hz, 1H), 4.30 (d, J = 6.3 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.2, 136.6, 136.2, 133.2, 129.0, 128.9, 128.9, 128.4, 127.9, 127.6, 126.5, 119.2, 117.5, 67.3, 52.4; IR (neat): 3087, 3063, 3033, 2948, 2929, 1705, 1597, 1496, 1455, 1399, 1294, 1275, 1218, 1137, 1005 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{20}NO_2$ 294.1494; Found 294.1504.

5-(3-iodopropen-1-yl)-3-phenyloxazolidin-2-one (19). To a solution of the *N*-1,3-pentadien-5-yl *N*-phenylcarbamate (0.341 g, 1.16 mmol) in CH_2Cl_2 (10 mL) under N_2 was added I_2 (0.589 g, 2.32 mmol). The dark brown solution was then stirred at ambient temperature under N_2 and reaction progress monitored by TLC (3:1 hexane/EtOAc). When the reaction was complete the mixture was diluted with CH_2Cl_2, poured into 10% aqueous $Na_2S_2O_3$, and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the

crude product. Chromatography over silica gel, eluting with 3:1 hexane/EtOAc and then EtOAc, afforded, after combining appropriate fractions and concentration under reduced pressure, 0.332 g (87%) of the title compound as a yellow/brown solid with mp 102-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.7 Hz, 2H), 7.35 (t, J = 7.4 Hz, 2H), 7.12 (t, J = 7.0 Hz, 1H), 6.15 (dt, J = 8.1, 7.6 Hz, 1H), 5.79 (dd, J = 8.6, 15.7 Hz, 1H), 5.04 (q, J = 7.6 Hz, 1H), 4.12 (t, J = 9.3 Hz, 1H), 3.85 (d, J = 8.1 Hz, 2H), 3.73 (dd, J = 7.4, 8.5 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.3, 138.0, 133.3, 129.1, 128.9, 124.2, 118.2, 72.11, 50.2, 2.3; IR (neat): 3063, 3048, 3032, 2952, 2889, 1749, 1598, 1503, 1404, 1372, 1219, 1136, 756 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{13}INO_2$ 329.9991; Found 329.9998.

***N*-1,2-butadien-4-yl *N*-Phenylcarbamate (20).** *Method A.* To a flame-dried 10 mL round bottom flask equipped with a condenser was added paraformaldehyde (0.075 g, 2.50 mmol), freshly purified CuI (0.095 g, 0.50 mmol), anhydrous 1,4-dioxane (5 mL), *N*-ethyn-3-yl *N*-Phenylcarbamate (**21**, 0.265 g, 1.00 mmol), and dicyclohexylamine (0.326 g, 0.358 mL, 1.80 mmol) under N_2. The resulting mixture was heated to reflux under N_2 and reaction progress was monitored by TLC (9:1 hexane/EtOAc). TLC analysis revealed the reaction to be complete after 2 h. The reaction mixture was cooled to ambient temperature, diluted with CH_2Cl_2 and H_2O, transferred to a separatory funnel and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude product as a green oil. Chromatography over silica gel, eluting with 9:1 hexane/EtOAc, afforded, after combining appropriate fractions and concentration under reduced pressure, 0.211 g (75%) of the title compound as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.37 (m, 10 H), 5.25 (quintet, J = 5.1 Hz, 1H), 5.17 (br s, 2H), 4.70 (dt, J = 6.5, 2.9 Hz, 2H), 4.27 (dt, J = 6.0, 6.0 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 208.9, 155.2, 142.0, 136.6, 128.9, 128.4, 127.9, 127.7, 126.9, 126.6, 87.3, 76.8, 67.3, 49.4; IR (ATR): 3063, 3031, 2937, 1955, 1698, 1597, 1494, 1396, 1271, 1214 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}NO_2$ 280.1338; found: 280.1344.

Method B. To a solution of benzyl *N*-phenylcarbamate (0.500 g, 2.20 mmol) in dry DMF (10 mL) under N_2 was added Cs_2CO_3 (2.150 g, 6.60 mmol), *n*-Bu_4NI (0.813 g, 2.20 mmol) and then 4-bromo-1,2-butadiene (0.878 g, 6.60 mmol).[21,22] The resultant mixture was stirred at ambient temperature under N_2 for 72 h. The reaction mixture was treated with H_2O (20 mL), and then extracted with 1:1 hexane/Et_2O (3 x 100 mL). The combined organic extracts were washed once with H_2O and brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product as a dark yellow oil. Chromatography of this residue over silica gel, eluting with 6:1 hexane/EtOAc, afforded, after combining appropriate fractions and concentration under reduced pressure, 0.470 g (77%) of the title compound as a yellow oil with spectral characteristics identical to those described above.

***N*-propyn-3-yl *N*-Phenylcarbamate (21).** To a cooled (5 °C) solution of benzyl *N*-phenylcarbamate (0.759 g, 3.34 mmol) in dry THF (50 mL) under N_2 was added NaH (60% dispersion in mineral oil, 0.147 g, 3.67 mmol) in small portions. After stirring for 30-60 min under N_2 the reaction mixture was first treated with *n*-Bu_4NI (0.135 g, 0.37 mmol) and then with propargyl bromide (80% in toluene, 0.522 g, 0.400 mL, 3.51 mmol). The cooling bath was then removed and the reaction mixture stirred at ambient temperature until TLC analysis (9:1 hexane/EtOAc) revealed the reaction to be complete. The reaction mixture was then cooled (5 °C) and carefully treated with H_2O (2 mL) to quench any unreacted NaH. The mixture was diluted with CH_2Cl_2 (50 mL), transferred to a separatory funnel and washed with H_2O (2 x 35 mL) and brine (35 mL). The organic layer was dried ($CaCl_2$), filtered and concentrated under reduced pressure to give the crude product. Chromatography over silica gel, eluting with 2:1 hexane/EtOAc, afforded, after combining appropriate fractions and concentration under reduced pressure, 0.853 g (96%) of the title compound as a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.42 (m, 10 H), 5.22 (s, 2H), 4.45 (d, J = 2.4 Hz, 2H), 2.24 (t, J = 2.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.9, 136.4, 129.0, 128.5, 128.0, 127.7, 127.1, 126.7, 79.6, 72.5, 67.6, 40.2; IR

(ATR): 3288, 3068, 3032, 2954, 2124, 1701, 1596, 1494, 1396, 1274, 1225 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}NO_2$ 266.1181; Found 266.1187.

5-(1-Iodoethen-1-yl)-3-phenyloxazolidin-2-one (22). To a solution of the *N*-1,2-butadien-4-yl *N*-Phenylcarbamate (**20**, 0.250 g, 0.895 mmol) in CH_2Cl_2 (10 mL) under N_2 was added I_2 (0.454 g, 1.79 mmol). The dark brown solution was then stirred at ambient temperature under N_2 and reaction progress monitored by TLC (3:1 hexane/EtOAc). After 19 hours, the mixture was diluted with CH_2Cl_2, poured into 10% aqueous $Na_2S_2O_3$, and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product as a dark yellow oil. Chromatography over silica gel, eluting with 3:1 hexane/EtOAc, afforded, after combining appropriate fractions and concentration under reduced pressure, 0.203 g (72%) of a white solid with mp 116-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, J = 1.1, 9.8 Hz, 2H), 7.37 (t, J = 8.1 Hz, 2H), 7.14 (t, J = 7.4 Hz, 1H), 6.63 – 6.64 (m, 1H), 6.01 – 6.02 (m, 1H), 4.90 (dd, J = 6.2, 9.0 Hz, 1H), 4.16 (t, J = 9.1 Hz, 1H), 3.80 (dd, J = 6.2, 9.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.8, 137.7, 129.1, 128.2, 124.4, 118.4, 106.9, 76.4, 50.9; IR (ATR): 3070, 3053, 2949, 2887, 1744, 1599, 1492, 1475, 1403, 1224, 1131, 756 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}INO_2$ 315.9835; Found 315.9842.

***N*-But-1-en-4-yl *N*-Phenylcarbamate (24).** To a solution of *N*-phenylaminobut-3-ene[25] (0.500 g, 3.40 mmol) in dry THF (20 mL) under Ar was added ground K_2CO_3 (0.820g, 3.92mmol) and, dropwise, benzyl chloroformate (0.610 g, 0.511 mL, 3.56 mmol) at ambient temperature. After stirring overnight, the reaction mixture was decanted from the potassium salts, which were washed using CH_2Cl_2 (25 mL). The organic layers were combined, washed with H_2O (2 x 15 mL), dried ($CaCl_2$), filtered and concentrated under reduced pressure to give a colorless liquid. Chromatography over silica gel, eluting with 100:15 hexane/EtOAc, provided, after combining appropriate fractions and concentration under

reduced pressure, 0.881 g (92%) of the title compound as an oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 – 7.37 (m, 10H), 5.68 – 5.78 (m, 1H), 5.13 (br s, 2H), 4.99 - 5.02 (m, 2H), 3.75 (t, J = 7.4 Hz, 2H), 2.29 (q, J = 7.2 Hz. 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ155.4, 141.7, 136.7, 135.0, 129.0, 128.3, 127.8, 127.5, 126.7, 116.8, 67.1, 49.8, 32.7; IR (neat): 3064, 3032, 2976, 2938, 1705, 1597, 1495, 1402, 1294, 1278, 1147 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{20}NO_2$ 282.1494; Found 282.1503.

Tetrahydro-6-(iodomethyl)-3-phenyl-1,3-oxazin-2-one (25). To $CHCl_3$ (6 mL) was added the *N*-buten-4-yl *N*-Phenylcarbamate (0.148 g, 0.526 mmol) and I_2 (0.160 g, 0.631 mmol) at ambient temperature under Ar. The resulting solution was stirred overnight under Ar. The reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with of 10% aqueous $Na_2S_2O_3$ (10 mL) and H_2O (10 mL), dried ($CaCl_2$), filtered and concentrated under reduced pressure to give a crude white solid. Chromatography over silica gel, eluting first with CH_2Cl_2 and then with 85:15 CH_2Cl_2/EtOAc, provided, after combining appropriate fractions and concentration under reduced pressure, 0.155 g (93%) of the title compound as a white crystalline solid with mp 145-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.38 (m, 2H), 7.23 – 7.28 (m, 3H), 4.40 (br s, 1H), 3.72 – 3.79 (m, 1H), 3.60 – 3.64 (m, 1H), 3.41 – 3.45 (m, 1H), 3.28 – 3.32 (m, 1H), 2.35 – 2.40 (m, 1H), 2.00 – 2.11 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ151.8, 142.4, 129.3, 127.0, 125.8, 76.4, 47.5, 27.7, 5.9; IR (neat): 3056, 2964, 2944, 2917, 1692, 1596, 1495, 1477, 1445, 1303, 1190, 1170, 755 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{13}INO_2$ 317.9991; Found 317.9998.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

^{1}H and ^{13}C NMR spectra for all new compounds, X-ray crystallographic data for compound **12** (PDF).

Further details on X-Ray data collection (experimental details, reflection statistics), as well as all crystallographic data are provided in .cif format. CCDC entry 1563634 contains the crystallographic data for structure **12**. This file can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033, or by e-mail: deposit@ccdc.cam.ac.uk.

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Notes

The authors declare no competing financial interest.

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