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Article

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Multi-Stereocenter-Containing Cyclopentanoids from Ynamides *via* Oxazolidinone Controlled Nazarov Cyclization.

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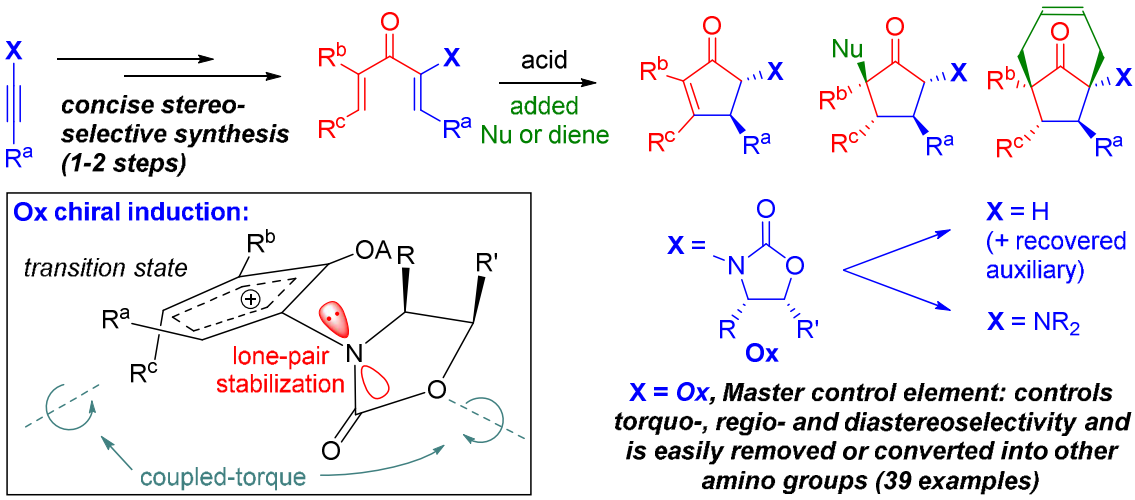
ABSTRACT

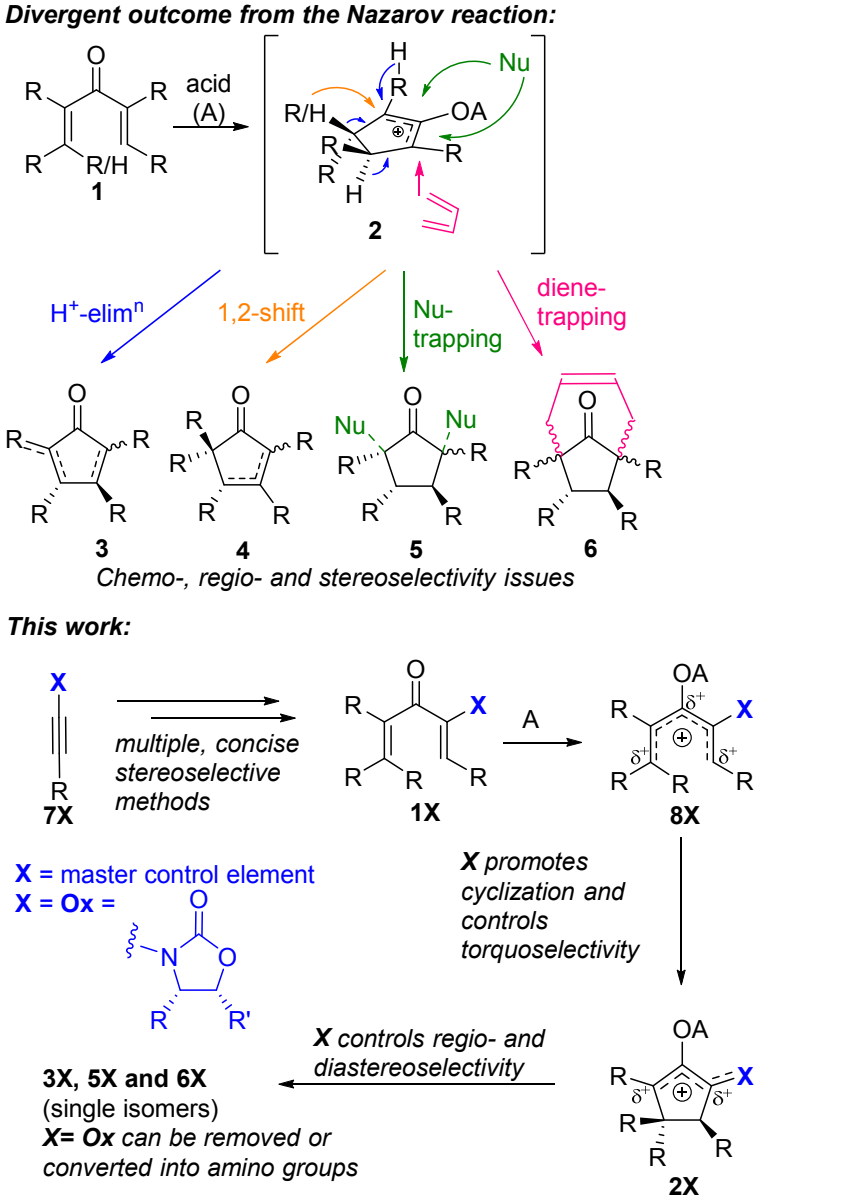


Achieving ready enantioselective access to multi-stereocenter containing cyclopentyl rings is an area of great significance to organic synthesis. In this work we describe a general protocol for accessing multi-stereocenter containing cyclopentanoids from simple *N*-alkynyloxazolidinones (**Ox**-ynamides). This protocol involves conversion of **Ox**-ynamides into **Ox**-activated divinyl and aryl vinyl ketones that undergo facile Nazarov cyclization with excellent chemo-, regio- and stereocontrol. The **Ox** auxiliary directs all aspects of reactivity and selectivity, both the electrocyclization and in the subsequent transformations of the resulting oxyallyl intermediate. Stereoinduction in the electrocyclization results from a "coupled-torque" mechanism where rotation of the **Ox** group, driven by increasing orbital overlap of the nitrogen lone pair with the incipient oxyallyl cation, is coupled with the rotation of the termini of the pentadienyl cation, favoring a particular direction of conrotatory ring closure (torquoselectivity). The associated lone-pair stabilization of the transition state by **Ox** promotes cyclization of traditionally resistant substrates, broadening the scope of this asymmetric Nazarov cyclization. The **Ox** group also facilitates the stereo- and regioselective incorporation of nucleophiles (Nu) and dienes, giving more complex, multi-stereocenter containing cyclopentanoid. Finally, the **Ox** group is readily removed and recovered or can be converted into other amine functionalities.

INTRODUCTION

Versatile methods for accessing cyclopentyl rings are highly desirable given the preponderance of cyclopentyl rings in bioactive natural products and the potential utility of cyclopentyl rings as sp^3-rich scaffolds in *de novo* drug design and compound-library screening.[1,2] Nazarov cyclizations of divinyl and aryl vinyl ketones **1** to give cyclopentenones and indenones **3** have attracted considerable attention as the basis for developing general methods for the enantioselective synthesis of cyclopentyl rings, which, if suitably controlled, could rival or even surpass the versatility that the Diels–Alder reaction holds for the synthesis of cyclohexyl rings (Scheme 1).[3,4] The Nazarov cyclization is potentially enriched by the number

of ways in which the reaction pathway can be terminated through the cationic intermediate **2**. Depending on the substitution pattern and the presence of suitable additives, cation **2** may undergo α-proton elimination to give **3**, [1,2]-sigmatropic shift to give **4**,[5] nucleophilic trapping to give **5**,[6] (4+3)-cycloaddition to give **6**[7] or a cationic reaction cascade to generate a polycycle (not shown).[8] In order to effectively harness this extraordinary potential of the Nazarov reaction in multi-stereocenter (sp^3-rich) scaffold synthesis, a number of challenges need to be overcome:[9] (i) concise stereoselective access to a structurally diverse array of substrates **1**; (ii) a capacity to cyclize conventionally resistant substrates; (iii) chemoselective control over the competing outcomes **3**-**6**; (iv) regiochemical control over the double-bond placement in **3**/**4** and of the Nu in **5**; and (v) control of relative and absolute stereochemistry in **3**-**6**. Herein, we describe our studies towards the identification of a master-control group **X** that can be readily incorporated into substrates **1X** from simple alkynes **7X** and which is highly effective in addressing the various chemo-, regio-, and stereoselectivity issues confronting the Nazarov reaction (Scheme 1).[10] These studies have identified Evans' oxazolidinone (**Ox**) as an excellent control element **X** (**X** = **Ox**) that promotes Nazarov cyclization of resistant substrates by stabilizing the charge redistribution (δ^+) in the transition state of the conversion of pentadienyl cation **8X** to (oxy)allylic cation **2X**. The **Ox** auxiliary has a strong influence on the torquoselectivty of the Nazarov reaction, resulting in essentially complete diastereoselectivity across a broad range of substrates. The charge stabilization afforded in **2X** by **X** = **Ox** strongly infuences its fate. It tends to favor regioselective proton elimination from **2X**, relative to [1,2]-shifts, and facilitates the regio- and stereoselective trapping of **2X** by nucleophiles and dienes. The **Ox** group is readily removed and recovered or can be further diversified by conversion into other amine functionalities.

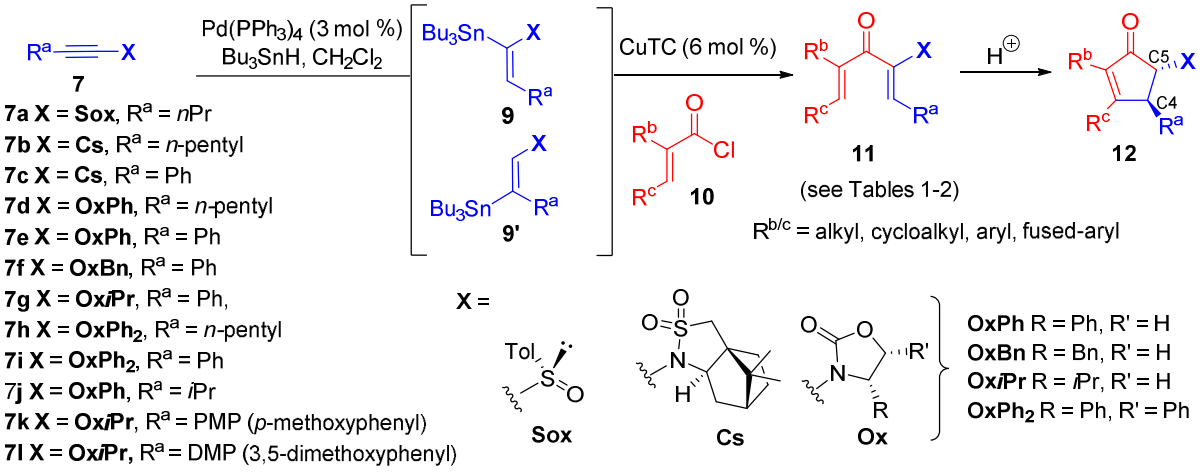


Scheme 1: Use of a master-control element **X** to achieve regio-, diastereo- and enantioselective control in the Nazarov reaction

RESULTS AND DISCUSSION

Identification of suitable control elements X: Since both electron-withdrawing and electron-donating groups **X** in **1X** have been proposed to be effective in promoting the Nazarov reaction, we examined both as chiral activating groups **X**.[11] The chiral sulfoxide (**X** = **Sox**) was employed as a chiral electron-withdrawing group while Oppolzer's camphorsultam (**X** = **Cs**) and several Evans' oxazolidinones (**X** = **Ox**) were employed as chiral electron-donating groups (Scheme 2). Ready access to aryl vinyl and divinyl ketones bearing **X** groups was achieved using a reductive-coupling protocol (Scheme 2).[12] This involves initial Pd-mediated hydrostannylation of the alkyne **7** followed by *in situ* cross-coupling to an acid chloride: **7** → **9** + **10** → **11**. A series of alkynes **7** bearing different groups **X** and R^a were intially coupled to tigloyl chloride **10** (R^b = R^c

= Me) for a preliminary evaluation of their synthetic utility in the formation of divinyl ketones **11** and for their capacity to induce torquoselectivity in the Nazarov cyclization to give **12** (Scheme 2 and Table 1). The regioselectivity of the hydrostannylation step in the reductive-coupling varied for the different alkynes **7**. The α-directing effect of the **X**-group dominated in all cases where R^a = alkyl, giving exclusively the desired regioiosmer **9**. However, since aryl groups are also α-directing groups in the Pd-mediated hydrostannylation of aryl alkynes, the capacity of **X** to favor **9** over **9'** in cases where R^a = aryl became an additional consideration in identifying preferred **X** groups. The order of the regioselectivity (ratio of **9**:**9'**) for the different **X** groups in the hydrostannylation of **7X** (R^a = Ar) was found to be **OxPh$_2$** ~ **Ox*i*Pr** (~9:1) > **OxBn** (~5:1) > **OxPh** (~3:1) >> **Cs** (~2:3).[13] The modest regioselectivities seen in the hydrostannylation of **7c** (**X** = **Cs**) (2:3) and **7e** (**X** = **OxPh**) (3:1) account for the lower yields achieved in their reductive-couplings with tigloyl chloride: **11c** (15%) and **11e** (51%), respectively (Table 1).



Scheme 2: Synthesis of various **X**-substituted divinyl ketones and their Nazarov cyclization products.

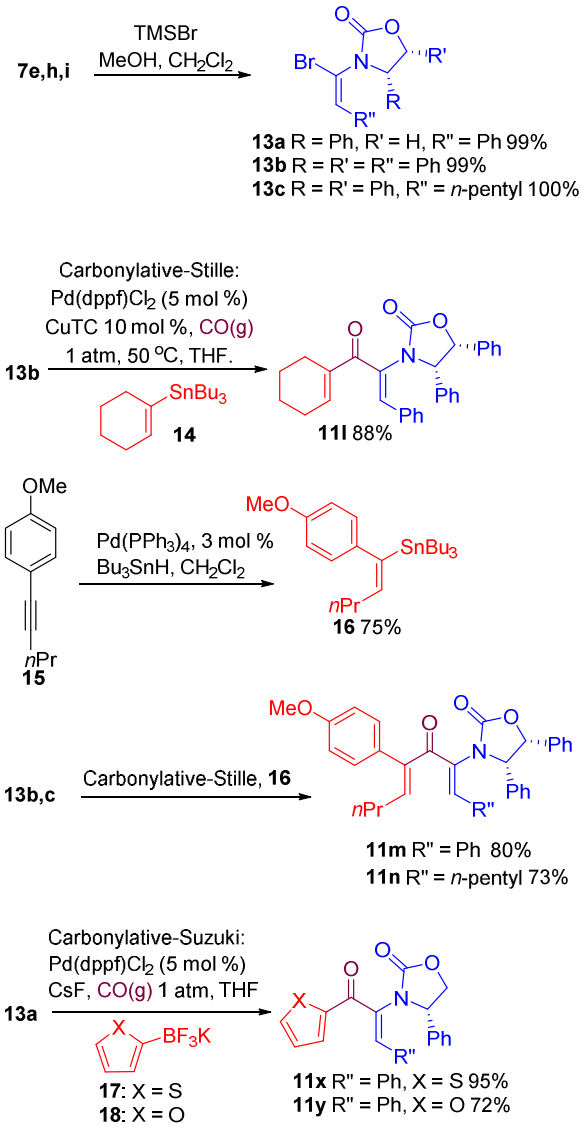
Table 1: Evaluation of Control Elements X

entry	7	X	R[a]	11, yield[a]	12, yield (dr)[b]
1	**7a**	**Sox**	*n*Pr	**11a**, 79%	no reaction
2	**7b**	**Cs**	*n*-pentyl	**11b**, 68%	**12b**, 80% (> 20:1)
3	**7c**	**Cs**	Ph	**11c**, 15%	**12c**, 99% (> 20:1)
4	**7d**	**OxPh**	*n*-pentyl	**11d**, 91%	**12d**, 99% (> 20:1)
5	**7e**	**OxPh**	Ph	**11e**, 51%	**12e**, 75% (> 20:1)
6	**7f**	**OxBn**	Ph	**11f**, 67%	**12f,** 85% (>20:1)
7	**7g**	**Ox*i*Pr**	Ph	**11g**, 83%	**12g**, 80% (> 20:1)
8	**7h**	**$OxPh_2$**	*n*-pentyl	**11h**, 93%	**12h**, 98% (> 20:1)
9	**7i**	**$OxPh_2$**	Ph	**11i**, 78%	**12i**, 84% (> 20:1)

[a] **11a-i** were formed by reductive-coupling with tigloyl choride **10** ($R^b = R^c$ = Me) see Scheme 2). [b] All reactions were performed using $MeSO_3H$ (10 equivalents) in CH_2Cl_2 at 0 ˚C–rt.

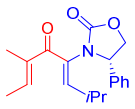
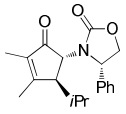
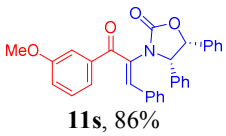
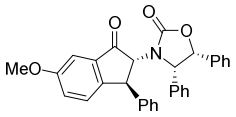
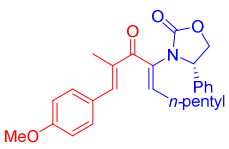
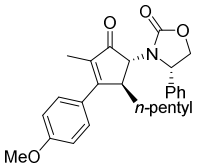
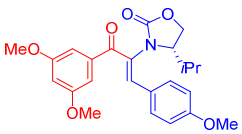
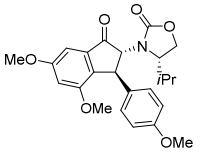
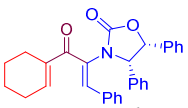
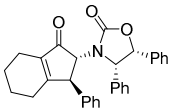
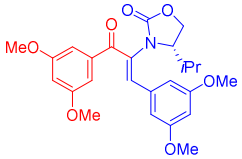
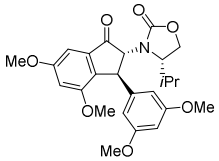
The Nazarov cyclizations of **11a-i** were undertaken using $MeSO_3H$ (10 equivalents = 1 M in CH_2Cl_2, 0 ˚C–rt) (Table 1). During the course of these studies, Salom-Roig and Sun reported the Nazarov cyclizations of some aryl vinyl and divinyl ketones bearing a chiral sulfoxide (**Sox**).[4d,e] These cyclizations require the involvement other electron-rich substituents in order to offset the electron-withdrawing nature of the sulfoxide.[4d,e] In the case of sulfoxide **11a**, which does not bear such an electron-donating group, no cyclization was observed under the conditions used in this study (1 M $MeSO_3H$ in CH_2Cl_2, rt, 24 h). By contrast, the chiral electron-donating **Cs** and **Ox** activated systems all cyclized efficiently (75-99% yield) with excellent diastereoselectivity favoring the C4β-stereochemistry [diastereomeric ratio (dr) > 20:1 (no C4α-diastereomer observable by ^{1}H NMR)]. While the substrate activation of **11b-i** by **Ox** and **Cs** is sufficient to enable cyclizations to be conducted at much lower temperatures (<0 ˚C) with catalytic amounts of acid (3 mol%), the higher acid concentrations (1 M) and sustained reaction at rt (24 h) were necessary to facilitate the epimerization at C5 to give exclusively the thermodynamically favored C4,C5-*trans* isomer. Much to our satisfaction, the cyclizations of divinyl ketones **11b-i** produced only one double-bond regioisomer **12b-i**, favoring placement of the double-bond distal to the auxiliary **X**. X-ray crystal structure analysis of **12c**, **12e** and a number of other products (**12j** and **23**, see below) confirmed the C4β-stereochemistry and all other isomers have also been assigned this stereochemistry.[10,13] In light of their superior utility in the reductive coupling protocol and their high levels of regio- and stereocontrol in the Nazarov reaction, **Ox** groups emerged as the preferred control elements **X** in the further development of this protocol.

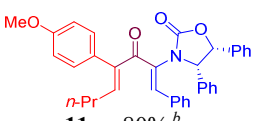
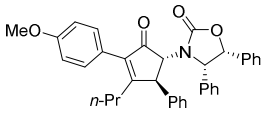
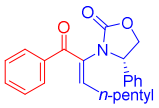
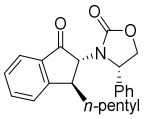
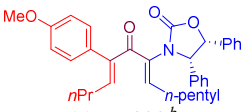
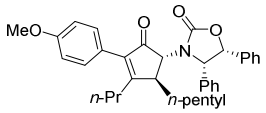
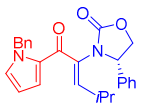
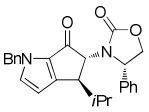
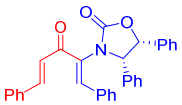
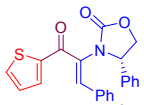
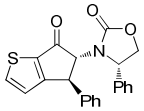
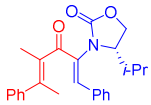
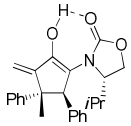
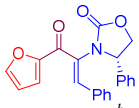
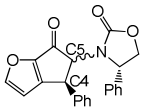
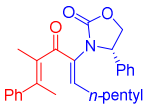
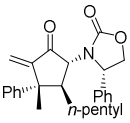
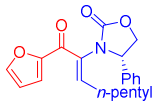
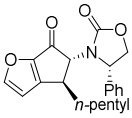
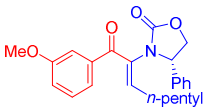
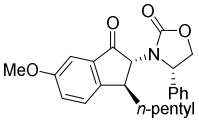
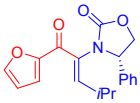
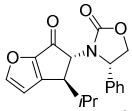
*Substituent variation in the **Ox**-controlled Nazarov cyclization:* A series of other divinyl and aryl vinyl ketones **11j-aa** containing **Ox** groups were accessed using either the reductive-coupling (Scheme 2) or a carbonylative cross-coupling protocol and were subjected to the Nazarov cyclization (Scheme 3 and Table 2; see legend for method of synthesis). Generally speaking, the reductive-coupling protocol worked well in all cases where it was applied (Table 2), except for those involving 2,3-dimethylcinnamoylchloride (Table 2 entries 7 and 8), which suffer from the increased steric hindrance asociated with the *cis*-methyl group. As a complement to hydrostannylation of **7**, the regio- and stereoselective hydrobromination of ynamides **7e**,**h**,**i** to give **13a-c** (99-100% yield) using TMSBr and MeOH in dichloromethane afforded access to Nazarov substrates **11** *via* carbonylative cross-coupling (Scheme 3). Carbonylative Stille coupling of **13b** with **14** to give **11l** (88%) was achieved using Pd(dppf)Cl_2 and copper 2-thiophenecarboxylate (CuTC) in THF under 1 atm of CO(g).[14] Hydrostannylation of the arylalkyne **15** to give **16** (75%), followed by carbonylative Stille cross-coupling of **16** with **13b** and **13c** gave **11m** (80%) and **11n** (73%), respectively, demonstrating a convergent synthesis of divinyl ketones **11** from two alkyne substrates (Scheme 2). While initial attempts to couple **13a** to arylboronic acids under standard, aqueous, carbonylative Suzuki-Miyaura conditions led only to the carboxylation of **13a** (not shown), we identified an alternative set of anhydrous conditions that could be performed at room temperature under just 1 atm of CO(g) using organotrifluoroboronate salts, CsF and Pd(dppf)Cl_2 in THF to give exclusively the coupled products **11x** (95%) and **11y** (72%).[15]



Scheme 3: Carbonylative coupling approaches to **Ox**-substituted divinyl ketones.

Table 2: Nazarov Cyclizations of Divinyl and Aryl Vinyl Ketones

entry	**7** + **10** → **11**, yield[a]	**12**, yield (dr)[c,d]	entry	**7** + **10** →**11**, yield[a]	**12**, yield (dr)[c,d]
1	 **11j**, 95%	 **12j**, 84%	10	 **11s**, 86%	 **12s**, 97%
2	 **11k**, 60%	 **12k**, 99%	11	 **11t**, 67%	 **12t**, 81%
3	 **11l**, 88%[b]	 **12l**, 85%	12	 **11u**, 75%	 **12u**, 92%

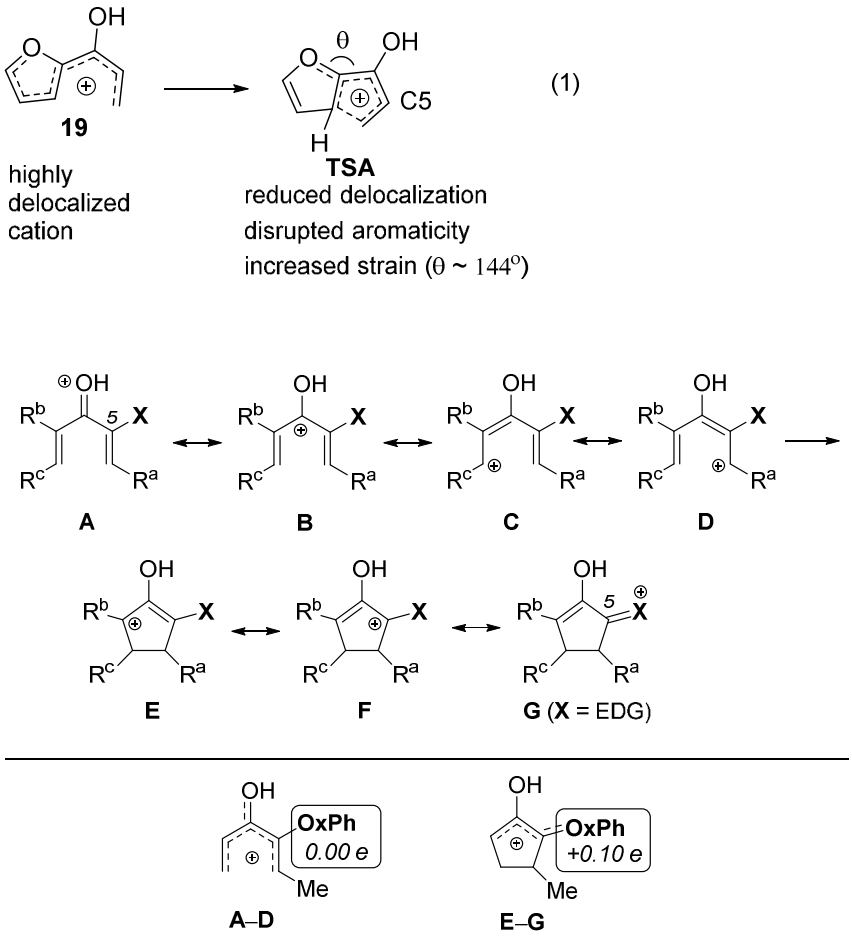
4	 **11m**, 80% [b]	 **12m**, 100%	13	 **11v**, 82%	 **12v**, 76%
5	 **11n**, 73% [b]	 **12n** 92%	14	 **11w**, 79%	 **12w**, 94%
6	 **11o**, 68%	Complex mixture	15	 **11x**, 95% [b]	 **12x**, 97%
7	 **11p**, 43%	 **12p**, 99%	16	 **11y**, 72% [b]	 **12y**, 82% [e]
8	 **11q**, not isol.	 **12q**, 45% from **7h**	17	 **11z** 61%	 **12z**, 79%
9	 **11r**, 87%	 **12r**, 90%	18	 **11aa**, 78%	 **12aa**, 25% [f]

[a] Unless otherwise stated, divinyl and and aryl vinyl ketones were formed by reductive-coupling (see Scheme 2). [b] Formed by carbonylative coupling (see Scheme 3). [c] Unless otherwise stated, all reactions were performed using $MeSO_3H$ (2-10 equivalents) in dichloromethane, 1,2-dichloroethane or toluene at rt or heating, depending on substrate (see Supporting Information for details). [d] Unless otherwise stated, all reactions proceeded with dr >20:1, with no other diastereomer observable by ^1H NMR. [e] Formed as a mixture of C5 epimers each with dr = 18:1. [f] Cyclized using 2 equivalents of TfOH in dichloromethane at 40 °C.

Nazarov cyclizations of divinyl ketones and aryl vinyl ketones depicted in Table 2 proceeded smoothly, except for **11o**, which gave a complex mixture of products (entry 6). Surprisingly, Nazarov cyclization of the same substrate, **11o**, in the presence of furan gave a good yield of furan-trapped product (see below), indicating that the Nazarov cyclization itself is facile but the product (or oxyallyl cation) are subject to further reaction under these conditions. As in the examples reported above in Table 1, the **Ox** group favors the C4β-stereochemistry (dr > 20:1) and the C4,5-*trans*-stereochemistry. The modest overall yield of **12q** (45% from ynamide **7h**) is associated with a low yield in the reductive-coupling step. In this case **11q** was not isolated but the crude reaction mixture resulting from reductive-coupling of **7h** and 2,3-dimethylcinnamoylchloride was treated directly with $MeSO_3H$. Again, as in the earlier examples, the regiochemical placement of the double bond in cyclopentenones **12j-q** is always to the distal side of the ring with respect to **Ox** (Table 1, entries 1-8).

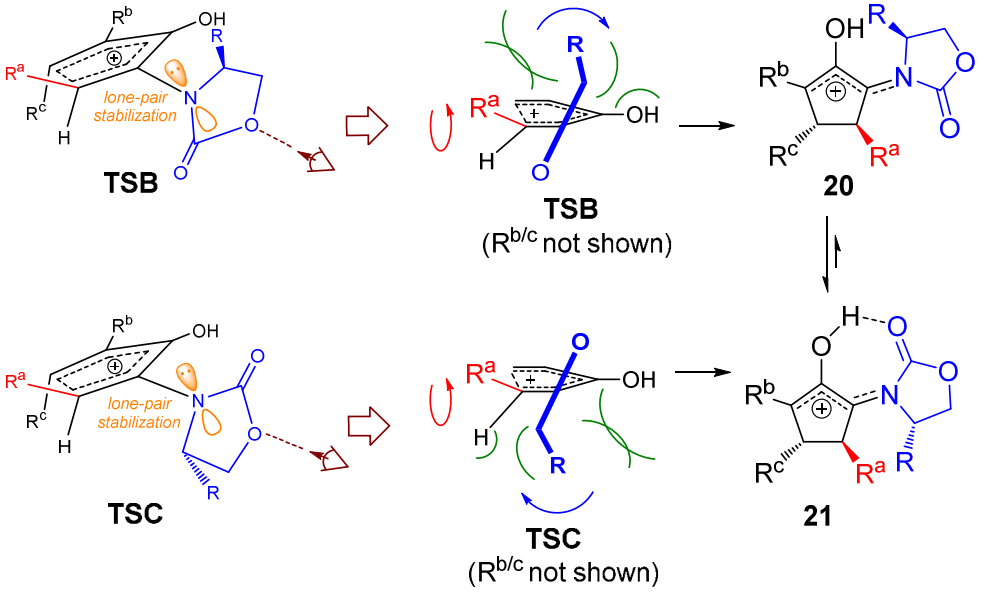
While the cyclizations of divinyl ketones were generally quite rapid, proceeding at < 0 ˚C, cyclizations of some aryl vinyl ketones were usually slower with some examples requiring moderate heating (40-80 ˚C). Importantly, the necessity to heat these Nazarov cyclizations had little effect on the level of chiral induction which remained high in all cases (dr > 20:1). For example, the cyclization of the phenyl vinyl ketone **11v**, which required 10 equivalents of $MeSO_3H$ in refluxing chloroform (65 ˚C) still afforded **12v** in 76% yield and dr > 20:1. Furan-2-yl vinyl ketones are well known to be resistant to Nazarov cyclization[16] and the cyclization of **11y** to **12y** (82%) and **11z** to **12z** (79%), the former at rt, are indicative of the powerful activating capacity of **Ox** in promoting the Nazarov reaction (Table 2 entries 16 and 17). While all other products could be isolated as a single C4,5-*trans* product after C5-epimerization, **12y** was resistant to C5-epimerization and attempts to achieve this through more forcing reaction conditions led to some C4 epimerization and loss of overall stereoinduction. Accordingly, **12y** was isolated as a mixture of C5-epimers. This inability to equilibrate **12y** to a single C5-epimer is of no consequence where the **OxPh** group is subsequently cleaved from the epimeric mixture to give a single product (see below).

Nazarov cyclization of isopropyl substituted furanyl vinyl ketone **11aa** was sluggish and required treatment with triflic acid (2 equivalents) in refluxing 1,2-dichloroethane (80 ˚C) to give **12aa** in low yield (25%) (Table 2, entry 18). Presumably the combination of the furan ring and a sterically hindering *i*Pr group combine to retard cyclization. This outcome stands in contrast to the corresponding pyrrole **11w**, which cyclized efficiently to **12w** (94%) upon treatment with 10 equivalents of $MeSO_3H$ in refluxing dichloromethane (40 ˚C). The resistance of furan-2-yl vinyl ketones to cyclization most likely arises from conflation of several factors (eq 1): (i) disruption of furan aromaticity; (ii) a significant reduction in charge stabilization (delocalization) in progression of **19** to the transition state **TSA** (eq 1); and accumulating strain in **TSA** due to a widened bond angle (θ~144˚). These effects are less pronounced in equivalent pyrrol-2-yl and thiophen-2-yl systems since the disruption in aromaticity is less in the case of the pyrrole and bond-angle strain is less in the case of the thiophene due to the large size of the sulfur atom. Presumably, the presence of the C5 **Ox** substituent (π-electron-donor) in the furan-2-yl vinyl ketones **11y** and **11z** compensates to some extent for these unfavorable features by increasing charge stabilization in **TSA**. In general, the Nazarov cyclization of a divinyl (or aryl vinyl) ketone has the effect of concentrating the positive charge as shown in Scheme 4. The positive charge is initially delocalized across the oxygen and five-carbons (resonance contributors **A**–**D**) but upon electrocyclization the charge is delocalized across a three-carbon system (resonance contributors **E** and **F**). An electron-donating substituent, such as **OxPh**, at the C5 position introduces the additional resonance contributor **G**. Calculations on the model system shown in Scheme 4 indicate that upon cyclization, about +0.1 *e* of positive charge is transferred onto the oxazolidinone as it comes into resonance with the oxyallyl cation.[13] The cyclization transition state (**D** → **E**) also derives stabilization from the incipient resonance stabilization by **X** = **OxPh**. In the model system, the **OxPh** substituent is calculated to lower the electrocyclization barrier by approximately 5 kcal/mol.[13]



Scheme 4: Charge-stabilization by **X** = EDG = **Ox**

We have previously examined the strong preference for the C4β-stereochemistry in the **Ox**-promoted Nazarov cyclization using density functional theory (DFT).[17] DFT calculations revealed that stereoinduction by **Ox** follows a unique "coupled-torque" mechanism. There are two low-lying transition states for the cyclization, wherein the **Ox** group adopts opposing conformations (**TSB** and **TSC**, Scheme 5). In both transition states, the **Ox** group exists at a relatively oblique angle (~40˚) with respect to the pentadienyl cation and, as the reaction proceeds further along the reaction coordinate, the **Ox** rotates (blue arrows) increasing orbital overlap of the electron-lone-pair on nitrogen with the emerging allylic π-cation in intermediates **20** and **21**. In each case, **TSB** → **20** and **TSC** → **21**, the sense of rotation of **Ox** is the same: clockwise. This unidirectional rotation by **Ox** minimizes steric clashing between the **Ox** R-group and the semi-planar pentadienyl cation. In turn, steric interactions between **Ox** and R^a determine the torquoselectivity of the conrotatory ring closure. The termini of the divinyl ketone rotate anticlockwise (red arrows), as this is the direction that minimizes clashing between R^a and the **Ox**-carbonyl (in **TSB**) or R^a and the **Ox**-CHR group (in **TSC**). Both cases lead to the same stereochemical outcome: the formation of the C4β stereoisomer.

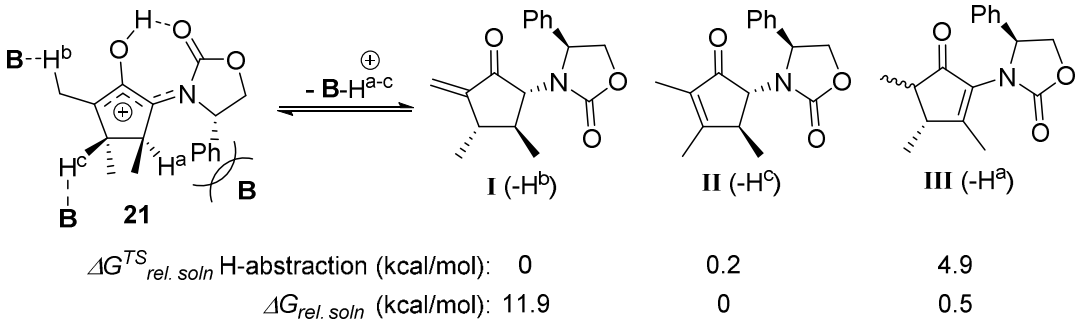


Scheme 5: "Coupled-torque" mechanism of chiral induction in the **Ox**-promoted Nazarov cyclization.

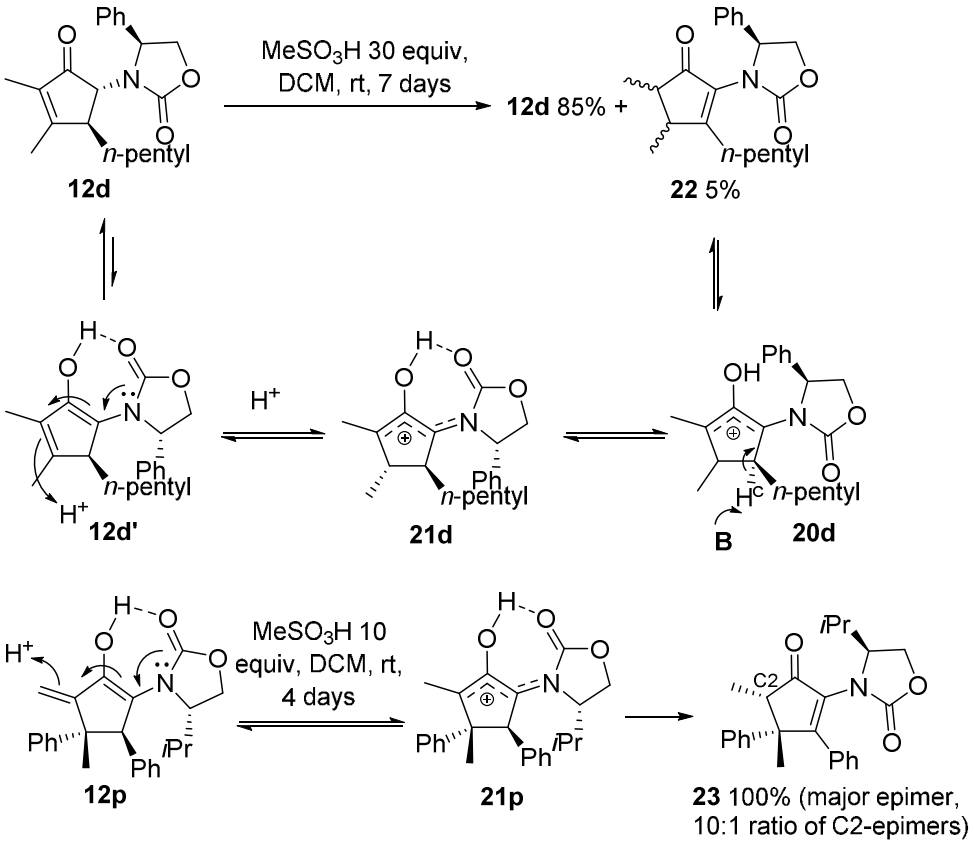
DFT calculations also explained the regioselectivity of the double-bond placement in the **Ox**-activated Nazarov cyclization (Scheme 6).[17] The double bond is consistently delivered to the distal side of the cyclopentenone ring with respect to **Ox** (**12d-q**). DFT calculations predicted that the intramolecularly H-bonded species **21** is the preferred conformation of the intermediate oxyallyl cation (Scheme 5). Assuming that the proton is transferred to another molecule acting as a base **B** (**B** = solvent, counter ion, substrate or product molecule), the calculations indicated that the preference for H^a, H^b or H^c-elimination (**I-III** respectively) is likely to result from a combination of thermodynamic and kinetic effects (Scheme 6). Kinetically, **I** and **II** are both favored over **III**, but thermodynamically **II-III** are favored over **I**. The strong preference for **II** observed experimentally can be rationalized as resulting from a rapid equilibration of the kinetically accessible isomers **I** and **II** through reversible formation of **21**, favoring **II** thermodynamically, under conditions where **III** is kinetically inaccessible.

To further explore the kinetic barriers to double-bond isomerisation, we treated **12d** with a large concentration of $MeSO_3H$ (5 M / 30 equivalents) for an extended period (Scheme 7). Under these conditions a small amount of the thermodynamic double-bond isomer **22** was detected by NMR after 7 days.[18] DFT calculations reveal that the relatively high barrier to H^a-abstraction arises from the steric effects imposed by the **Ox** substituent in **21**, which blocks access to H^a by the base **B** (Scheme 6). Abstraction of H^a requires that the **Ox** group adopt a higher energy conformation involving loss of H-bonding, i.e. **21d** → **20d** (Scheme 7). The necessity to form the enol **12d'** in order to re-access the allylic cation **21d** is also likely to contribute to the low rate of equilibration of **12d** and **22**. Double bond isomerization of **12p** was also studied (Scheme 7). In this case, reformation of the allylic cation **21p** is more facile due to the higher electron denisty in the double bond in **12p**. Nonetheless, its conversion to the thermodynamically preferred isomer **23** was still very slow, being notable only after 16 h and complete after 4 days. By contrast, Nazarov cyclization of **11p** to **12p** is complete in < 5 min under these conditions. **23** was obtained as a 10:1 mixture of C2 Me-epimers,

favoring the C2α-epimer as determined by X-ray crystallography.[13] The experimental studies Scheme 7 are consistant with our earlier theoretical studies (Scheme 6)[17] demonstrating significant kinetic barriers to H^a-abstraction during the Nazarov reaction, which are responsible for the regioselectivity favoring **I**/**II** over **III**. These barriers are important, because although the **Ox**-promoted Nazarov cyclization to form cyclopentenones is very fast (usually complete within minutes), the epimerization at C5 is slower, requiring up to 1-2 h in the presence of 3-10 equivalents (0.3-1.0 M) of $MeSO_3H$. Thus, the low barrier for the conversion **I** → **II**, the thermodynamic preference for **II** relative to **I**, and the significant thermodynamic difficulty associated with formation of **III** ensure that Nazarov cyclization of **11Ox** to **12Ox** can be achieved under conditions that enable thermodynamic equilibration of the **Ox** group to the lower energy *trans*-isomer **II** without competing double-bond isomerisation of **II** to **III**. Of additional significance is that no [1,2]-sigmatropic shifts were observed in these Nazarov cyclizations, even in cases where the group adjacent to the oxyallyl cation has a relatively high migratory aptitude, such as the Me and Ph groups attached to the quaternary center in **12p** and **12q**. This is attributed to the **Ox**-stabilization of the allylic cation, disfavoring the formation of higher energy cations via [1,2]-migration. This further underscores the master-control role played by the **Ox** auxiliary in ensuring a predictable, chemoselective outcome.



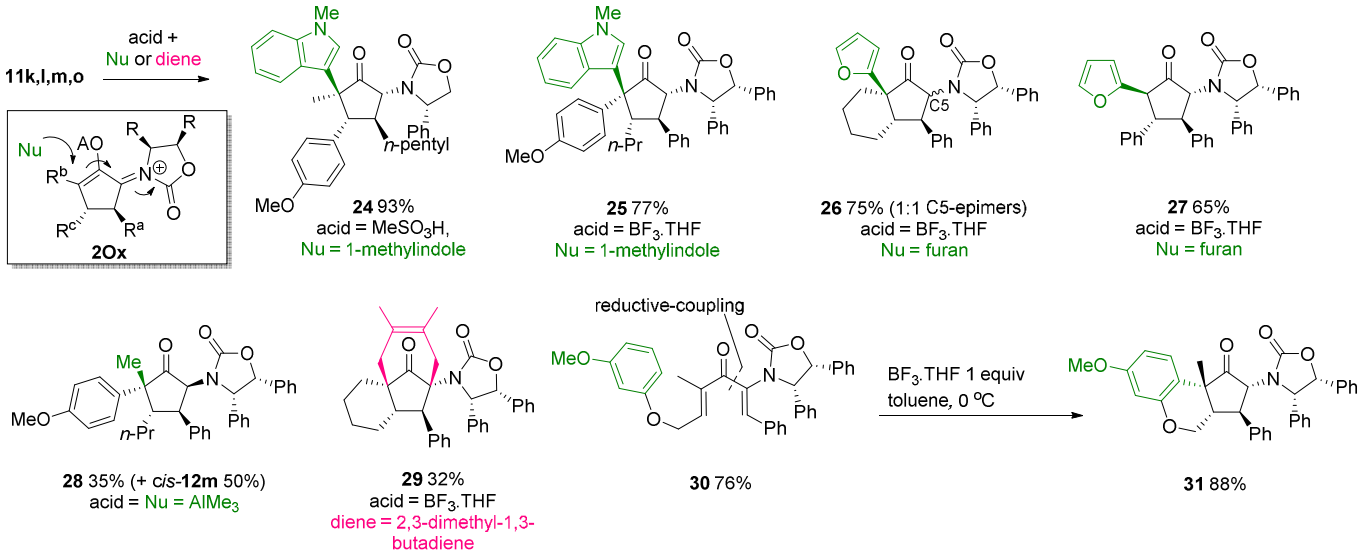
Scheme 6: **Ox**-directed regioselective placement of the double-bond.[17]



Scheme 7: Thermodynamic double-bond isomerisation of **12d** and **12o**

Oxyallyl Cation Trapping: One of the most significant innovations in the Nazarov cyclization has been the effective trapping of the intermediate oxyallyl cations with a range of nucleophiles and dienes.[5-7] We have investigated the utility of the **Ox**-promoted Nazarov cyclization for the regio- and stereoselective incorporation of nucleophiles and dienes [alkylation, arylation, or (4+3)-cycloaddition] (Scheme 8). Nazarov cyclizations of **11k** and **11m** in the presence of *N*-methyl indole and of **11l** and **11o** in the presence of furan gave exclusively the trapped products **24** (93%), **25** (77%), **26** (75%) and **27** (65%), respectively.[19] West and coworkers have previously shown that the use of $AlMe_3$ as a Lewis acid in the Nazarov cyclization results in oxyallyl cation trapping through methyl transfer from aluminium.[6d] Cyclization of **11m** with $AlMe_3$ afforded a modest yield of the trapped material **28** (35%), which was isolated as the kinetically favored *cis*-isomer, plus a significant amount of the cyclopentenone ***cis*-12m**. The **Ox**-group plays a key role in the regioselectivity of these intermolecular trapping reactions, favoring a 1,4-type addition to the α,β-unsaturated **Ox**-iminum ion **2Ox** (Scheme 7 box). At first glance, the stereochemistry of Nu incorporation might appear to be attributed to steric interations between Nu and the neighbouring α-R^b group of **2Ox**; however, computational studies of the furan-trapping suggest that the stereoselectivity depends on CH–π interactions (see below). Trapping of **11l** with 1,3-butadiene produced the (4+3)-cycloadduct **29** in modest yield (32%). Lastly, intramolecular trapping of a tethered arene was achieved upon treatment of **30** (accessed in 76% yield by reductive-coupling)[13] with BF_3.THF to give **31** (88%). These trapping reactions

have enabled four new continguous stereocenters to be generated enantioselectively, including chiral quaternary stereocenters.



Scheme 8: Oxyallyl trapping of nucleophilies and dienes

The trapping of furan in **26** and **27** by a Friedel–Crafts reaction rather than a (4+3)-cycloaddition is in contrast to previous studies, which have suggested that stabilized oxyallyl cations arising from Nazarov cyclizations are biased towards asynchronous (4+3)-cycloadditions with furans, whereas less stabilized, more electrophilic, oxyallyl cations prefer to undergo nucleophilic trapping.[7d] It also contrasts with other studies on the reactions of furans with acyclic **Ox**-stabilized oxyallyl intermediates, which led to (4+3) cycloadducts.[20] To gain a better understanding of the factors controlling the chemo- and stereoselectivity of the trapping of furans in the **Ox**-controlled Nazarov reaction, we performed DFT calculations. Computations with M06-2X[21] were performed on the reaction of furan with oxyallyl intermediate **2o** (**X** = **OxPh$_2$**, A = BF_3) which leads to **27** (Figure 1). The computations show that the transition states for addition of furan to the top and bottom faces of **2o** (**TSD** and **TSE**, respectively) differ in energy by 1.0 kcal/mol ($\Delta\Delta G^{\ddagger}$) favoring addition to the top (β) face.[13] Although the molecular conformations of **TSD** and **TSE** resemble those of (4+3)-cycloaddition transition states,[20c,d] the products contain only one C–C bond, i.e. the bond between furan and C2 of oxyallyl **2o**. The interaction between furan and C5 of **2o** in the TS is stabilizing but does not lead to bond formation. This result is similar to that reported by West *et al.*[7d] in their DFT studies on non-stabilized oxallyl cations. Computations predict that ring closure of the C2(β)–furan-trapped intermediate via formation of a bond to C5, which would lead to a (4+3)-cycloadduct, has a barrier ($\Delta G^{\ddagger}$) of 21.3 kcal/mol, which is 5.7 kcal/mol higher than the barrier for the first C–C bond-forming step (15.6 kcal/mol, **TSD**) (see the Supporting Information). This provides the opportunity for the initially formed furan-trapped intermediate to undergo deprotonation leading to **27**, rather than ring closure leading to the (4+3)-cycloadduct. The stereoselectivity of the addition of furan to **2o** can be traced to CH–π interactions

occurring within the transition states. The TS for addition to the β face (**TSD**) contains a CH–π interaction between furan and **OxPh$_2$** whereas the TS for addition to the bottom face (**TSE**) contains a CH–π interaction between furan and the C3-Ph group of **2o**. The phenyl rings involved in these CH–π interactions are highlighted in blue in Figure 1. In **TSD**, H3 of the furan lies 2.79 Å from the center of the nearby Ph ring of **OxPh$_2$**, while in **TSE**, H2 of the furan lies 3.04 Å from the center of the nearby Ph ring of **2o**. The stronger CH–π interaction in **TSD** explains the lower energy of **TSD**, which leads to the preference for the formation of the C4β product. Related CH–π interactions have previously been observed in both nucleophilic and cycloaddition pathways of oxyallyl trapping,[7d,20c] including the aforementioned (4+3)-cycloadditions of furans to acyclic **Ox**-stabilized oxyallyl cations.[20a]

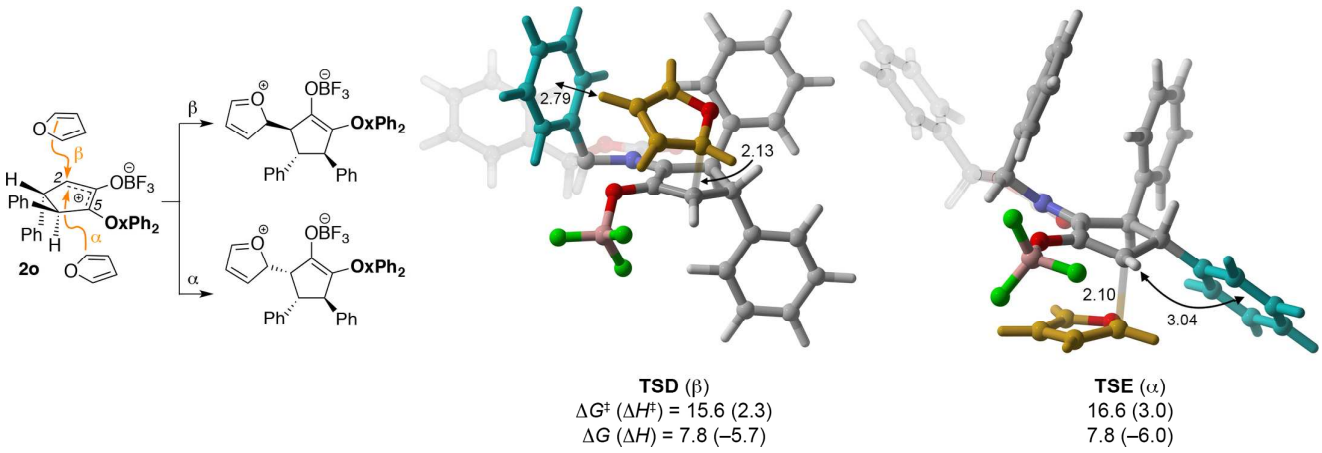
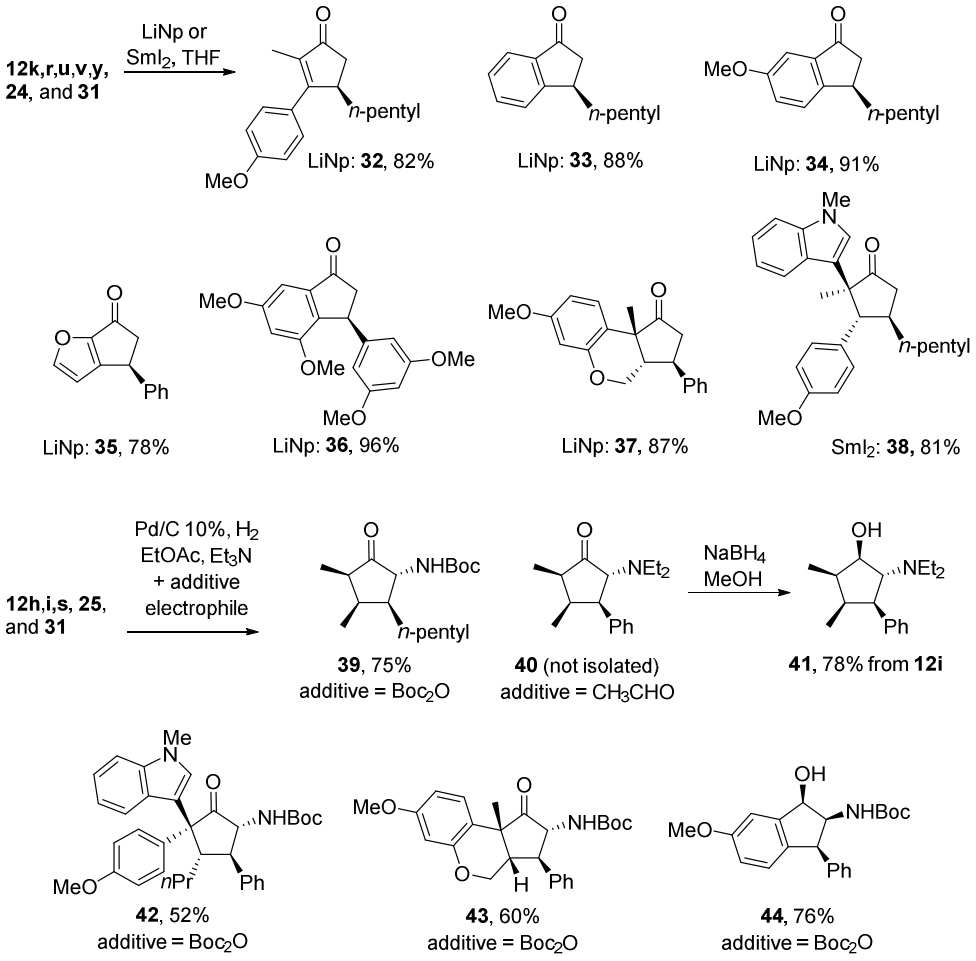


Figure 1: Transition states for addition of furan (highlighted in gold) to the α or β face of oxyallyl intermediate **2o** (**X** = **OxPh$_2$**, A = BF_3), computed with M06-2X/6-311+G(d,p)-SMD(CH_2Cl_2)//M06-2X/6-31G(d). Distances in Å. Energies (kcal/mol) are reported with respect to **2o** plus furan.

A*uxiliary cleavage:* The **Ox** group can be cleaved using either lithium naphthalenide (LiNp) or SmI_2 as demonstrated for a sample set of Nazarov cyclization products **12**, **24**, and **31** giving the **32-38** in good yields (78-96%) (Scheme 9). If desired, the cleaved **Ox** group can be recovered from these reactions for recycling, adding to the atom efficiency of the protocol. The diphenyloxazolidinone **OxPh$_2$** also serves as a masked amine, which can be revealed upon Pd/C hydrogenation (Scheme 9).[22] Since the Nazarov cyclization products contain a ketone, it proved necessary to perform these hydrogenations in the presence of an electrophile (Boc_2O or CH_3CHO) in order to avoid the formation of dimers and oligomers through reductive-amination reactions. Accordingly, a sample set of **OxPh$_2$**-containing Nazarov products **12**, **25** and **31** was converted to a series of substituted amines **39-44** (52-78%). In the case of **12h** and **12i**, the double-bond was also stereoselectively hydrogentated to give **39** (75%) and **40**, respectively. Isolation of **40** proved difficult as the product was prone to decomposition during chromatography; however, diastereoselective reduction of the ketone with $NaBH_4$ gave the more stable alcohol **41**, which was isolated in 78% yield from

12i. The stereochemistry of **41** was assigned by NOESY NMR, revealing that the stereoselective delivery of the hydrogen from hydrogenation (Pd/C, H_2) and the hydride from $NaBH_4$ had occurred from the bottom face. Hydrogenation of **12s** to give **44** (76%) is presumed to involve stereoselective hydrogenation of the enol tautomer of **12s** to give a hydroxyl group, followed by hydrogenation of **$OxPh_2$**. This explanation is supported by the observation that both the pure *trans*-isomer **12s** (formed under conditions of thermodynamic control) and a mixture of *cis*-and *trans*-**12s** (formed under conditions of kinetic control) both gave the same product, **44**, upon hydrogenation. The stereochemistry of **44** is tentatively assigned as all *cis*, assuming that delivery of the hydrogen to the enol occurs from the face opposite the C4-Ph group.



Scheme 9: **Ox**-group removal or elaboration

CONCLUSION

The stereoselective *syn*-hydrostannylation and *syn*-hydrobromination of readily accessible ynamides **7**, in conjunction with palladium-mediated coupling techniques (in particular reductive-coupling and carbonylative-coupling), provides concise, stereoselective access to a range of aryl vinyl and divinyl ketones **11**. The **Ox** group has emerged as a highly effective, multi-functional, master-control element in the Nazarov cyclization, enabling access to a broad range of cyclopentanoid structures with high levels of

chemo-, regio- and stereoselectivity. The capacity of the **Ox** group to alleviate the otherwise unfavorable charge-concentrating effect of the Nazarov cyclization (**8X** → **2X**, Scheme 1) through nitrogen lone-pair donation in **2Ox**, enables it to be effectively employed in the cyclization of traditionally resistant substrates, such as furan-2-yl vinyl ketones (**19** → **TSA**, eq 1). The **Ox** in the oxyallyl intermediate **2Ox** also plays a critical role in controlling the regioselectivity of double-bond formation or nucleophilic trapping, and in avoiding competing [1,2]-sigmatropic shifts. The **Ox-**groups can be reductively cleaved from the products and recycled or, in the case of **$OxPh_2$**, converted into other amine functionalities by hydrogenation (Scheme 9). In short, the **Ox**-controlled Nazarov cyclization represents a broadly applicable method for the synthesis of enantiopure, multi-stereocenter containing cyclopentanoids from readily accessible **Ox**-ynamides.

EXPERIMENTAL

General: All experiments were performed under an anhydrous atmosphere of nitrogen in flame-dried glassware except as indicated. Melting points were recorded with an electrothermal melting point apparatus. Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded at 400 MHz for proton and 100 MHz for carbon nuclei. All NMR spectra were recorded in (D)chloroform ($CDCl_3$) at 30 °C. The protonicities of the carbon atoms observed in the carbon NMR were determined using J-modulated spin-echo (jmod) experiments. High-resolution mass spectra (HRMS) were recorded on a time of flight mass spectrometer fitted with either an electrospray (ESI) or atmospheric pressure ionization (APCI) ion source. Tetrahydrofuran (THF) and dichloromethane (DCM), were purified using a commercial Solvent Purification System. Analytical and preparative TLC were conducted on aluminium backed 0.2 mm thick silica gel 60 GF254 plates and the chromatograms were visualized under a 254 nm U.V. lamp and/or by treatment with a reagent solution [phosphomolybdic acid / 95% ethanol (4g: 100mL) dip] or anisaldehyde dip (214 mL EtOH, 8 mL H_2SO_4, AcOH 2.4 mL, anisaldehyde 5.9 mL) followed by heating. Flash column chromatography was performed using silica 40 - 63 micron. The synthesis and spectral data of the following compounds has been previously reported: **7d**,**e**,**g**,**j**,[10] **7l**,[23] **11d**,**e**,**g**,**j**,**k**,**p**,**v-z**,[10] **11u**,[23] **12d**,**e**,**g**,**j**,**k**,**p**,**v-z**,[10] **12u**,[23] **13a**,[10] **16**,[10] **24**,[10] and **32-38**[10].

General Method A, Copper(II) Catalyzed Ynamide Formation:

Using a modification of the procedure previously described.[24] A mixture of camphorsultam or oxazolidinone (NH-substrate) (1.0 equivalent), ground K_2CO_3 (2.0 equivalents), ground $CuSO_4.H_2O$ (0.1 equivalents), 1,10-phenanthroline (0.2 equivalents) and bromoalkyne (1.2 equivalents) in toluene (1 M in NH-substrate) was heated at 90 °C until ^{1}H NMR (aliquot) indicated complete consumption of the NH-substrate, typically 24-48 h. After this time the reaction was cooled to rt, filtered through Celite (rinsing with EtOAc), concentrated under reduced pressure and chromatographed.

General Method B, Reductive-Coupling:

To a stirred solution of alkyne **7** (1.0 equivalent) and $Pd(PPh_3)_4$ (3-5 mol%) in dichloromethane (0.1 - 0.2 M, relative to **7**) at 0 °C was added Bu_3SnH (1.05 equivalents) dropwise over 2 minutes. The solution was then warmed to RT over 0.5 h and to it were added sequentially the acid chloride **10** (1.0 - 1.2 equivalents) and copper(I) thiophenecarboxylate (CuTC) or CuCl (10 mol%). The reaction mixture was stirred until TLC revealed complete consumption of the intermediate vinylstannane (2-16 h, typically run overnight). The solvent was removed under reduced pressure and the residue dissolved in Et_2O (or EtOAc for solubility). KF solution (20% w/v, aq.) was added and the resultant mixture stirred for 1-2 h. The liquid phases were separated (some solid particulate matter may remain suspended in the organic phase, presumably Bu_3SnF, which is removed upon later filtration) and the aqueous phase was re-extracted twice with Et_2O (or EtOAc). The combined organic extracts were dried over $MgSO_4$, concentrated under reduced pressure and the crude product purified by flash chromatography.

General Method C, Nazarov Reaction:

$MeSO_3H$ (10 equivalents) was added to a stirred solution of divinyl or aryl vinyl ketone **11** in dichloromethane (0.1-0.2 M) at 0 °C, the reaction mixture was then allowed to warm to rt over 1 h. After this time the reaction was monitored by TLC until completion then quenched by careful addition saturated $NaHCO_3$ aq. solution. The mixture was transferred to a separatory funnel and the phases separated. The aqueous phase was extracted twice with dichloromethane, the combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Where necessary, the crude compounds were purified by flash chromatography.

General Method D, Reductive Cleavage of Ox:

Lithium naphthalenide solution (0.7-1.0 M, ~2 equivalents, freshly prepared from addition of lithium metal into a solution naphthalene in THF) was added dropwise to a stirred solution of **Ox-**cyclopentanoid (1.0 equilavent) in THF (0.05-0.1 M) at -78 °C until the dark color persisted. The reaction was quenched at -78 °C by addition of saturated aqueous NH_4Cl solution. After warming to rt the reaction mixture was partitioned between Et_2O and H_2O and the aqueous phase was re-extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography.

General Method E, Hydrogenation of $OxPh_2$:

Triethylamine (3 drops) and the desired electrophile (Boc anhydride or acetaldehyde) (5 equivalents) was added to a solution of **$OxPh_2$-**cyclopentanoid (1 equivalent) in EtOAc or THF (0.1 M in cyclopentanoid) and Pd/C (10%) (1:1 weight ratio with cyclopentanoid). The reaction mixture was evacuated and back-filled with hydrogen three times and stirred at rt for 2 days. After this time the reaction filtered through Celite (rinsing with EtOAc), concentrated under reduced pressure and chromatographed.

(3a*S*,6*R*,7a*R*)-1-(Hept-1-yn-1-yl)-8,8-dimethylhexahydro-1*H*-3a,6-methanobenzo[*c*]isothiazole 2,2-dioxide (7b)

Prepared according to General Method A using (1*S*)-(−)-2,10-camphorsultam (754 mg, 3.5 mmol), 1-bromo-1-heptyne (674 mg, 3.85 mmol), $CuSO_4.H_2O$ (62 mg, 0.35 mmol), 1,10-phenanthroline (126 mg, 0.70 mmol) and K_2CO_3 (967 mg, 7.0 mmol) in toluene (3.5 mL). Flash chromatography (silica gel, 12:88 EtOAc/hexanes) gave the title compound **7b-CS** as a thick oil (939 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.51 (dd, *J* = 7.8, 4.2 Hz, 1H), 3.21 (s, 2H), 2.29 (t, *J* = 6.9 Hz, 2H), 2.18 (m_c, 1H), 1.95-1.82 (m, 3H), 1.74 (dd, *J* = 13.5, 8.1 Hz, 1H), 1.52 (pent., *J* = 7.2 Hz, 2H), 1.42 (m_c, 1H), 1.47-1.25 (m, 5H), 1.10 (s, 3H), 0.93 (s, 3H), 0.89 (t, *J* = 6.9 Hz, 3H). This NMR spectra is consistent with that previously reported.[25]

(3a*S*,6*R*,7a*R*)-8,8-Dimethyl-1-(phenylethynyl)hexahydro-1*H*-3a,6-methanobenzo[*c*]isothiazole 2,2-dioxide (7c)

Prepared according to General Method A using (1*S*)-(−)-2,10-camphorsultam (754 mg, 3.5 mmol), 1-bromo-2-phenylethyne (697 mg, 3.85 mmol, from phenylacetylene), $CuSO_4.H_2O$ (62 mg, 0.35 mmol), 1,10-phenanthroline (126 mg, 0.70 mmol) and K_2CO_3 (967 mg, 7.0 mmol) in toluene (3.5 mL). Flash chromatography (silica gel, 15:85 EtOAc/hexanes) gave the title compound **7c** as a low-melting solid (991 mg, 90%). ^{1}H NMP (400 MHz, $CDCl_3$) δ 7.40 (δ, *J* = 3.9 Hz, 2H), 7.27 (s, 3H), 3.64 (δδ, *J* = 7.8, 3.9 Hz, 1H), 3.27 (s, 2H), 2.24 (d, *J* = 12.9 Hz, 1H), 1.95-1.72 (m, 4H), 1.42 (m_c, 1H), 1.26 (m_c, 1H), 1.12 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7 (CH), 128.3 (CH), 128.0 (CH), 122.8 (C), 77.1 (C), 72.7 (C), 67.3 (CH), 51.3 (C), 49.9 (CH_2), 48.0 (C), 44.5 (CH), 34.5 (CH_2), 31.6 (CH_2), 27.1 (CH_2), 20.3 (CH_3), 20.0 (CH_3). This NMR spectra is consistent with that previously reported.[25]

(*S*)-4-Benzyl-3-(phenylethynyl)oxazolidin-2-one (7f)

Prepared according to General Method A (*S*)-4-benzyloxazolidin-2-one (1.42 g, 8.00 mmol), 1-bromo-2-phenylethyne (1.73 g, 9.56 mmol, from phenylacetylene), $CuSO_4.H_2O$ (142 mg, 0.80 mmol), 1,10-phenanthroline (288 mg, 1.60 mmol) and K_2CO_3 (2.21 g, 16.0 mmol) in toluene (8 mL). Flash chromatography (silica gel, 2:49:49 Et_2O/DCM /hexanes) gave the title compound **7f** as a white solid (1.82 g, 82%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (m_c, 2H), 7.39-7.22 (m, 8H), 4.42-4.31 (m, 2H), 4.18 (m_c, 1H), 3.30 (dd, *J* = 14.0, 3.7 Hz, 1H), 3.02 (m_c, 1H). This NMR spectra is consistent with that previously reported.[26]

(4*S*,5*R*)-3-(Hept-1-yn-1-yl)-4,5-diphenyloxazolidin-2-one (7h)

Prepared according to General Method A (4S,5R)-4,5-diphenyloxazolidin-2-one (1.0 g, 4.18 mmol), 1-bromoheptyne (0.946 g, 5.44 mmol, from 1-heptyne), $CuSO_4.H_2O$ (66.7 mg, 0.418 mmol), 1,10-phenanthroline (150.8 mg, 0.837 mmol) and K_2CO_3 (1.154 g, 8.362 mmol) in toluene (5 mL). Flash chromatography (silica gel, 2:48:48 Et_2O/DCM/hexanes) gave the title compound as a thick oil (1.142 g, 82%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.18 – 7.04 (m, 6H), 6.98 – 6.83 (m, 4H), 5.91 (d, *J* = 8.2 Hz, 1H), 5.29 (d, *J* = 8.2 Hz, 1H), 2.18 (t, *J* = 7.0 Hz, 2H), 1.43 – 1.30 (m, 2H), 1.22 – 1.09 (m, 4H), 0.79 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7, 133.6, 133.0, 128.6, 128.44, 128.2, 128.1, 127.6, 126.2, 80.7, 72.56, 69.6, 67.2, 30.8, 28.32, 22.1, 18.4, 134.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{24}NO_2^+$: 334.1802. Found: 334.1804.

(4*S*,5*R*)-4,5-Diphenyl-3-(phenylethynyl)oxazolidin-2-one (7i)

Prepared according to General Method A (4S,5R)-4,5-diphenyloxazolidin-2-one (3 g, 12.552 mmol), 1-bromo-2-phenylethyne (2.83 g, 15.64 mmol), $CuSO_4.H_2O$ (200 mg, 1.29 mmol), 1,10-phenanthroline (452 mg, 2.51 mmol) and K_2CO_3 (3.46 g, 25.07 mmol) in toluene (15 mL). Flash chromatography (silica gel, 2:48:48 Et_2O/DCM/hexanes) gave the title compound as a white solid (3.80 g, 90%). MP = 158.2-162.3. ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (dddd, *J* = 7.4, 5.8, 4.0, 1.5 Hz, 5H), 7.14 (ddd, *J* = 9.6, 5.2, 2.0 Hz, 6H), 6.96 (dt, *J* = 7.6, 3.0 Hz, 4H), 5.99 (d, *J* = 8.1 Hz, 1H), 5.44 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 133.4, 132.8, 131.7, 128.8, 128.6, 128.4, 128.3, 128.2, 128.2, 127.6, 126.2, 122.2, 81.1, 78.6, 72.5, 67.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{18}NO_2^+$: 340.1332. Found: 340.1335.

(*S*)-4-Isopropyl-3-[(4-methoxyphenyl)ethynyl]oxazolidin-2-one (7k)

Prepared according to General Method A (*S*)-4-isopropyloxazolidin-2-one (1.21 g, 9.39 mmol), 1-(bromoethynyl)-4-methoxybenzene (2.08 g, 9.86 mmol), $CuSO_4.H_2O$ (167 mg, 0.94 mmol), 1,10-phenanthroline (339 mg, 1.88 mmol) and K_2CO_3 (2.60 g, 18.8 mmol) in toluene (9.4 mL). Flash chromatography (silica gel, 3:49:48 Et_2O/DCM/hexanes) gave the title compound **7k** as a white solid (1.48 g, 61%). MP = 121-123 ˚C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 4.41 (t, *J* = 9.0 Hz, 1H), 4.19 (dd, *J* = 9.0, 5.8 Hz, 1H), 4.03 (ddd, *J* = 8.8, 5.8, 4.1 Hz, 1H), 3.81 (s, 3H), 2.29 (septet.d, *J* = 6.9, 4.1 Hz, 1H), 1.03 (d, *J* = 6.9 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5 (C), 156.0 (C), 133.1 (CH), 114.1 (C), 113.7 (CH), 77.0 (C), 71.7 (C), 64.7 (CH_2), 61.9 (CH), 55.1 (CH_3), 29.1 (CH), 17.0 (CH_3), 15.1 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{18}NO_3^+$: 260.1281. Found: 260.1278.

(4*S*,5*R*)-3-((*E*)-1-bromo-2-phenylvinyl)-4,5-diphenyloxazolidin-2-one (13b):

Prepared as for **13a** above: TMS-Br (221.29 mg, 1.445 mmol), MeOH (0.058 mL, 1.445 mmol), (4*S*,5*R*)-4,5-diphenyl-3-(phenylethynyl)oxazolidin-2-one **7i** (500 mg, 1.474 mmol) in DCM (10 mL), gave **13b** 99% (610 mg, 100%) as white solid. Mp 138.6-142.8. IR: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 2.8 Hz, 5H), 7.14 – 7.01 (m, 4H), 6.95 (s, 1H), 6.86 (dd, *J* = 10.9, 4.7 Hz, 4H), 6.44 (d, *J* = 7.3 Hz, 2H), 5.80 (d, *J* = 8.4 Hz, 1H), 5.42 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7, 136.9, 134.3, 134.3, 131.7, 128.9, 128.8, 128.6, 128.6, 128.5, 128.4, 128.0, 127.9, 126.1, 116.7, 80.2, 67.3. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{19}BrNO_2^+$: 420.0594. Found: 420.0588.

(4*S*,5*R*)-3-((*E*)-1-bromohept-1-en-1-yl)-4,5-diphenyloxazolidin-2-one (13c):

Prepared as for **13a** above: TMS-Br (150.03 mg, 0.98 mmol), MeOH (0.0395 mL, 0.98 mmol), **7h** (333 mg, 1 mmol) in DCM (7 mL) gave **13c** (410 mg, 100%) as a thick oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.00 (m, 6H), 6.95 (dd, *J* = 6.3, 2.8 Hz, 2H), 6.89 – 6.76 (m, 2H), 5.96 – 5.81 (m, 2H), 5.45 (d, *J* = 8.6 Hz 1H), 2.29 – 1.91 (m, 2H), 1.51 – 1.03 (m, 6H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.80, 153.9, 134.7, 133.0, 128.5, 128.4, 128.23, 128.1, 126.6, 126.2, 80.39, 62.8, 35.8, 31.636, 28.8, 24.3, 22.6, 14.1. HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{25}NO_2Br^+$: 414.1063. Found 414.1063.

(2*E*,5*Z*)-3-Methyl-5-[(*S*)-*p*-tolylsulfinyl]nona-2,5-dien-4-one (11a)

Prepared according to General Method B using alkynyl sulfoxide **7a**[27] (103 mg, 0.500 mmol), $Pd(PPh_3)_4$ (16 mg, 0.014 mmol), Bu_3SnH (140 μL, 0.500 mmol), tigloyl chloride (0.50 mmol) and CuCl (40 mg, 0.40 mmol) in THF (3.5 mL). Flash chromatography (silica gel, 84:16 hexane / EtOAc) yielded the title compound **11a** as a discoloured oil (114 mg, 79%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 6.60 (t, *J* = 7.7 Hz, 1H), 6.42 (q, *J* = 7.1 Hz, 1H), 2.37 (s, 3H), 2.14 (app. q, J_{app} = 7.4 Hz, 2H), 1.75 (d, *J* = 7.1 Hz, 3H), 1.62 (s, 3H), 1.49 (app. sext, J_{app} = 7.3 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (JMOD, 75 MHz, $CDCl_3$) δ 193.5 (C), 145.4 (C), 144.8 (CH), 141.9 (C), 139.08 (C), 139.07 (C), 137.6 (CH), 129.7 (CH), 125.1 (CH), 31.7 (CH_2), 22.0 (CH_2), 21.4 (CH_3), 15.0 (CH_3), 13.7 (CH_3), 10.3 (CH_3). LRMS *m/z* (%): 313.2 (40, $M+Na^+$), 291.2 (100, MH^+). IR (cm^{-1}): 2959, 2929, 1632, 1242, 1083, 1055, 809. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{22}NaO_2S^+$: 313.1238. Found: 313.1235.

(2*E*,5*Z*)-5-[(3a*S*,6*R*,7a*R*)-8,8-Dimethyl-2,2-dioxidohexahydro-1*H*-3a,6-methanobenzo[*c*]isothiazol-1-yl]-3-methylundeca-2,5-dien-4-one (11b)

Prepared according to General Method B using ynamide **7b** (464 mg, 1.5 mmol), DCM (15 mL), $Pd(PPh_3)_4$ (87 mg, 0.075 mmol), Bu_3SnH (0.42 mL, 1.58 mmol), tigloyl chloride (181 μL, 1.65 mmol) and CuTC (29 mg, 0.15 mmol). Flash chromatography (silica gel, 12:88 EtOAc/hexanes) gave the title compound as a low melting solid (404 mg, 68%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (m_c, 1H), 6.28 (dd, *J* = 8.8, 6.4 Hz, 1H),

3.86 (dd, *J* = 7.8, 4.2 Hz, 1H), 3.16 (s, 2H), 2.44 (m_c, 1H), 2.32 (m_c, 1H), 1.83-1.74 (m, 10H), 1.54 (dd, *J* = 12.0, 8.0 Hz, 1H), 1.45-1.35 (m, 2H), 1.32-1.17 (m, 6H), 1.15 (s, 3H), 0.87 (s, 3H), 0.80 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0 (C), 147.4 (CH), 139.7 (CH), 137.7 (C), 129.4 (C), 64.9 (CH), 49.83 (C), 49.76 (CH_2), 47.3 (C), 44.5 (CH), 35.1 (CH_2), 32.2 (CH_2), 31.4 (CH_2), 28.6 (CH_2), 28.5 (CH_2), 26.6 (CH_2), 22.1 (CH_2), 20.5 (CH_3), 19.9 (CH_3), 14.5 (CH_3), 13.7 (CH_3), 11.9 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{36}NO_3S^+$: 394.2410. Found: 394.2412.

(1*Z*,4*E*)-2-[(3a*S*,6*R*,7a*R*)-8,8-Dimethyl-2,2-dioxidohexahydro-1*H*-3a,6-methanobenzo[*c*]isothiazol-1-yl]-4-methyl-1-phenylhexa-1,4-dien-3-one (11c)

Prepared according to General Method B using ynamide **7c** (473 mg, 1.5 mmol), DCM (15 mL), $Pd(PPh_3)_4$ (87 mg, 0.075 mmol), Bu_3SnH (0.420 mL, 1.58 mmol), tigloyl chloride (181 μL, 1.65 mmol) and CuTC (29 mg, 0.15 mmol). Flash chromatography (silica gel, hexanes/toluene/EtOAc) gave the title compound **11c** as a white solid (91.2 mg, 15%). Mp 143-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 4.0 Hz, 2H), 7.40-7.28 (m, 3H), 6.90 (s, 1H), 6.88 (q, *J* = 7.2 Hz, 1H), 3.70 (br. s, 1H), 3.19 (s, 1H), 1.89 (s, 3H), 1.87 (d, *J* = 7.2 Hz, 3H), 1.85-1.55 (m, 4H), 1.33 (m_c, 1H), 1.15 (s, 3H), 1.05-0.90 (m, 3H), 0.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0 (C), 143.4 (CH), 137.9 (C), 133.1 (C), 129.7 (C), 129.4 (CH), 128.9 (CH), 127.9 (CH, 2C), 65.6 (CH, broad), 50.6 (C), 49.8 (CH_2), 47.5 (C), 44.3 (CH), 35.0 (CH_2), 32.7 (CH_2), 26.6 (CH_2), 20.4 (CH_3), 20.3 (CH_3), 15.0 (CH_3), 11.7 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{30}NO_3S^+$: 400.1941. Found: 400.1944.

(*S*)-4-Benzyl-3-[(1*Z*,4*E*)-4-methyl-3-oxo-1-phenylhexa-1,4-dien-2-yl]oxazolidin-2-one (11f)

Prepared according to General Method B using ynamide **7f** (418 mg, 1.51 mmol), DCM (10 mL), $Pd(PPh_3)_4$ (52 mg, 0.045 mmol), Bu_3SnH (0.43 mL, 1.58 mmol), tigloyl chloride (144 μL, 1.31 mmol) and CuTC (29 mg, 0.15 mmol). Flash chromatography (silica gel, 17:82:1 EtOAc/hexanes/Et_3N) gave the title compound **11f** as a white solid (366 mg, 67%). MP = 130-132 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (m_c, 2H), 7.48-7.38 (m, 3H), 7.19-7.12 (m, 3H), 7.00 (s, 1H), 6.77 (m_c, 2H), 6.66 (qq, *J* = 6.9, 1.3 Hz, 1H), 4.25 (m_c, 1H), 4.17-4.06 (m, 2H), 2.81 (dd, *J* = 13.6, 4.5 Hz, 1H), 2.65 (dd, *J* = 13.6, 9.5 Hz, 1H), 1.94 (m_c, *J* < 1.3 Hz, 3H), 1.88 (dq, *J* = 6.9, 1.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ194.2 (C), 156.8 (C), 140.9 (CH), 137.0 (C), 135.63 (C), 135.56 (CH), 133.2 (C), 132.4 (C), 129.7 (CH), 129.3 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 126.8 (CH), 68.4 (CH_2), 56.2 (CH), 38.4 (CH_2), 14.7 (CH_3), 12.3 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{24}NO_3^+$: 362.1751. Found: 362.1758.

(4*S*,5*R*)-3-((2*E*,5*Z*)-3-Methyl-4-oxoundeca-2,5-dien-5-yl)-4,5-diphenyloxazolidin-2-one (11h)

Prepared according to General Method B using ynamide **7h** (1.00 g, 3.003 mmol), DCM (30 mL), $Pd(PPh_3)_4$ (173 mg, 5 mol%), Bu_3SnH (0.848 mL, 3.15 mmol), tigloyl chloride (395 μL, 3.609 mmol) and CuTC (57.26 mg, 0.3 mmol). Flash chromatography (silica gel, 12:88 EtOAc/hexanes) gave the title compound **11h** as a thick oil. (1.158 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 – 6.92 (m, 8H), 6.80 – 6.70 (m, 2H), 6.23 (dd, *J* = 8.9, 5.6 Hz, 1H), 5.93 (d, *J* = 8.7 Hz, 1H), 5.68 (qd, *J* = 6.9, 1.4 Hz, 1H), 5.53 (d, *J* = 8.7 Hz, 1H), 2.47 – 2.17 (m, 2H), 1.76 – 1.68 (m, 3H), 1.61 (dd, *J* = 6.9, 1.1 Hz, 3H), 1.52 – 1.38 (m, 1H), 1.36 – 1.16 (m, 5H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.0, 156.2, 144.8, 138.5, 137.1, 135.4, 134.2, 132.7, 128.7, 128.5, 128.1, 128.0, 126.1, 79.8, 64.7, 31.9, 29.1, 28.0, 22.5, 14.5, 14.1, 12.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{27}H_{32}NO_3^+$: 418.2377. Found: 418.2381.

(4*S*,5*R*)-3-((1*Z*,4*E*)-4-Methyl-3-oxo-1-phenylhexa-1,4-dien-2-yl)-4,5-diphenyloxazolidin-2-one (11i)

Prepared according to General Method B using ynamide **7i** (678 mg, 2.5 mmol), DCM (20 mL), $Pd(PPh_3)_4$ (115.55 mg, 0.1 mmol), Bu_3SnH (0.565 mL, 2.1 mmol), tigloyl chloride (241 μL, 2.193 mmol) and CuTC (38.13 mg, 0.2 mmol). Flash chromatography (silica gel, 19:81 EtOAc/hexanes) gave the title compound **11i** as a low melting solid. 424.191 (658 mg, 78%). MP = 65.6-67.5. IR: NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 5H), 7.15 – 7.10 (m, 3H), 6.98 (ddd, *J* = 9.7, 4.0, 1.5 Hz, 3H), 6.84 (dd, *J* = 13.5, 6.0 Hz, 3H), 6.53 (dd, *J* = 8.2, 1.0 Hz, 2H), 6.35 (qd, *J* = 6.9, 1.3 Hz, 1H), 5.83 (d, *J* = 8.8 Hz, 1H), 5.41 (d, *J* = 8.7 Hz, 1H), 1.87 – 1.85 (m, 3H), 1.76 (dd, *J* = 6.9, 1.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.91, 156.77, 140.57, 137.36, 135.8, 135.3, 133.6, 132.9, 132.2, 129.5, 129.5, 128.7, 128.6, 128.2, 128.1, 127.869, 127.6, 126.3, 80.4, 65.0, 14.8, 12.5. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{28}H_{26}NO_3^+$: 424.1907. Found: 424.1910.

Tributyl(cyclohex-1-en-1-yl)stannane (14)

t-BuLi (1.31 M in pentane, 5.7 mL, 7.45 mmol) was added slowly to a solution of 1-bromocyclohex-1-ene (0.42 mL, 3.726 mmol) and anhydrous THF (6.2 mL) at −78 ˚C and the reaction stirred for 1 h at −78 °C. Bu_3SnCl (1.1 mL, 3.912 mmol) was slowly added and the reaction allowed to warm to rt and stir for 18 h. K_2CO_3 aq. (10% w/v, 12 mL) was added to the reaction and the mixture extracted with Et_2O (2 x 12 mL), washed with H_2O (2 x 12 mL) and brine (2 x 12 mL) then dried over $MgSO_4$ and concentrated under reduced pressure yielding tributyl(cyclohex-1-en-1-yl)stannane as colourless liquid (1.33 g, 96%). ^{1}H NMR (401 MHz, $CDCl_3$) δ 5.79 (m, 1H), 2.20 – 2.10 (m, 2H), 2.09 – 1.99 (m, 2H), 1.66 – 1.57 (m, 4H), 1.53 – 1.42 (m, 6H), 1.37 – 1.25 (m, 6H), 0.92 – 0.81 (m, 15H).[28]

(4*S*,5*R*)-3-((*Z*)-3-(Cyclohex-1-en-1-yl)-3-oxo-1-phenylprop-1-en-2-yl)-4,5-diphenyloxazolidin-2-one (11l)

Bromoenamide **13b** (461.6 mg, 1.10 mmol), cyclohexenyl stannane **14** (530 mg, 1.4277 mmol), Pd(dppf)Cl_2 (44.8 mg, 0.0549 mmol), CuTC (20.9 mg, 0.11 mmol) and anhydrous THF (11 mL) were added to flamed dried round bottom flask. Reaction was evacuated and backfilled with CO(g) for 3 times then heat to 50 ^oC overnight. Reaction was then diluted with water (15 mL) and extracted with EtOAc (2 x 15 mL), wash with water (2 x 15 mL) and brine (2 x 15mL), dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (NEt_3 treated silica gel, 15:85 EtOAc/hexanes) yielded the title compound **11l** as an off white syrup (432.3 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$) δ7.40-7.38 (m, 3H), 7.32-7.29 (m, 2H), 7.11-7.09 (m, 3H), 6.98-6.94 (m, 3H), 6.84-6.81 (m, 3H), 6.56-6.54 (m, 1H), 6.52 (dd, *J*= 8.17, 0.97 Hz, 2H), 5.82 (d, *J*= 8.77Hz 1H), 5.39 (d, *J*= 8.75Hz 1H), 2.57-2.51 (m, 1H), 2.17-2.03 (m, 3H), 1.68-1.57 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ193.1, 156.8, 143.19, 138.6, 135.6, 135.3, 133.7, 132.8, 132.2, 129.5, 129.4, 128.7, 128.6, 128.2, 128.1, 127.9, 127.6, 126.3, 80.5, 65.0, 26.1, 24.1, 22.0, 21.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}NO_3^+$: 450.2064. Found 450.2058.

(4*S*,5*R*)-3-((1*Z*,4*E*)-4-(4-Methoxyphenyl)-3-oxo-1-phenylocta-1,4-dien-2-yl)-4,5-diphenyloxazolidin-2-one (11m)

To a solution of bromoenamide **13b** (700 mg, 1.67 mmol) in THF (20 mL), the vinyl stannane **16** (1012 mg, 2.171 mmol) was added along with CuTC (31.9 mg, 0.167 mmol) and Pd(dppf)Cl_2 (68.2 mg, 0.083 mmol). The reaction was heated for 15 h at 50 ^oC under an atmosphere of CO (g) (balloon) after which time TLC revealed complete consumption of **13b**. The reaction mixture was diluted with water and extracted with EtOAc, dried over $MgSO_4$, evaporated in vacuo and chromatographed (silica gel, 30% EtOAc in hexane) giving the product as a yellow solid (728 mg, 80.2%). MP = 114.8-118.2. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.28 (m, 5H), 7.10 (dd, *J* = 8.4, 4.8 Hz, 4H), 7.05 – 6.92 (m, 5H), 6.91 – 6.74 (m, 4H), 6.50 (d, *J* = 7.2 Hz, 2H), 6.30 (t, *J* = 7.5 Hz, 1H), 5.85 (d, *J* = 8.7 Hz, 1H), 5.55 (d, *J* = 8.7 Hz, 1H), 3.78 (s, 3H), 2.16 (ddd, *J* = 14.7, 7.3, 1.5 Hz, 2H), 1.37 (h, *J* = 7.4 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 158.9, 157.2, 143.8, 140.4, 139.6, 135.2, 133.3, 133.0, 133.0, 130.6, 129.8, 129.6, 128.6, 128.5, 128.3, 128.2, 128.0, 127.8, 127.7, 126.2, 113.7, 80.2, 65.3, 55.2, 31.5, 22.4, 13.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{36}H_{34}NO_4^+$: 544.2482. Found: 544.2486.

(4*S*,5*R*)-3-((4*E*,7*Z*)-5-(4-Methoxyphenyl)-6-oxotrideca-4,7-dien-7-yl)-4,5-diphenyloxazolidin-2-one (11n) Prepared according to the procedure described for **11m**: bromoenamide **13c** (400 mg, 0.969 mmol), vinyl stannane **16** (587 mg, 1.26 mmol), CuTC (18.4 mg, 0.10 mmol), Pd(dppf)Cl_2 (40 mg, 0.48 mmol) and THF (10 mL). Flash chromatography (silica gel, 30% EtOAc in hexane) gave the product **11n** as a thick oil (380 mg, 73.1%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 – 6.90 (m, 8H), 6.73 (dt, *J* = 20.9, 6.5 Hz, 6H), 6.37 (dd, *J* = 9.4, 4.9 Hz, 1H), 5.98 – 5.83 (m, 2H), 5.77 (d, *J* = 8.7 Hz, 1H), 3.75 (s, 3H), 2.45 – 2.30 (m, 1H), 2.20 (tt, *J* = 14.7, 7.3 Hz, 1H), 2.05 (q, *J* = 7.5 Hz, 2H), 1.38 – 0.93 (m, 8H), 0.81 (dt, *J* = 12.3, 7.3 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.4, 192.9, 158.82 156.40 147.7, 142.45 140.40, 135.46134.3, 133.4, 130.4, 128.8, 128.5, 128.3, 128.1, 128.0, 128.0, 126.0, 113.7, 79.8, 64.6, 55.2, 31.7, 31.3, 30.7, 30.5, 30.3, 30.1, 29.9, 29.18, 27.9, 22.57, 22.4, 14.0, 13.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{35}H_{40}NO_4^+$: 538.2952. Found: 538.2956.

(4*S*,5*R*)-3-((1*Z*,4*E*)-3-Oxo-1,5-diphenylpenta-1,4-dien-2-yl)-4,5-diphenyloxazolidin-2-one (11o)

Prepared according to General Method B using ynamide **7i** (300 mg, 0.884 mmol), $Pd(PPh_3)_4$ (30.6 mg, 0.027 mmol), Bu_3SnH (0.23 mL, 0.884 mmol), cinnamoyl chloride (147.3 mg, 0.884 mmol), CuTC (10.1 mg, 0.0530 mmol) DCM (4.4 mL). Flash chromatography (silica gel, 15:85 EtOAc / hexanes) yielded **11o** as yellow oil (284.2 mg, 68%). ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.72 (d, *J* = 15.7 Hz, 1H), 7.56 (dd, *J* = 6.7, 2.8 Hz, 2H), 7.47 – 7.37 (m, 9H), 7.21 (d, *J* = 15.7 Hz, 1H), 7.15 – 7.08 (m, 3H), 7.01 – 6.94 (m, 3H), 6.81 (t, *J* = 7.8 Hz, 2H), 6.46 (d, *J* = 7.2 Hz, 2H), 5.88 (d, *J* = 8.7 Hz, 1H), 5.46 (d, *J* = 8.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.8, 157.5, 145.3, 137.9, 135.2, 134.7, 134.3, 133.4, 132.8, 130.7, 130.0, 129.6, 129.0, 128.7, 128.7, 128.6, 128.3, 128.1, 127.9, 127.7, 126.2, 121.4, 80.5, 65.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{32}H_{26}NO_3^+$: 472.1907. Found 472.1907.

(*S*,*Z*)-3-[1-(3-Methoxyphenyl)-1-oxooct-2-en-2-yl]-4-phenyloxazolidin-2-one (11r)

Prepared according to General Method B using ynamide **7d** (515 mg, 2.0 mmol), DCM (10 mL), $Pd(PPh_3)_4$ (116 mg, 0.10 mmol), Bu_3SnH (0.56 mL, 2.1 mmol), 3-methoxybenzoyl chloride (310 µL, 2.2 mmol) and CuTC (38.2 mg, 0.10 mmol). Flash chromatography (silica gel, 18:82 EtOAc/hexanes) gave the title compound as a thick oil (687 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.02 (ddd, *J* = 8.3, 2.7, 0.9 Hz, 1H), 6.87-6.83 (m, 2H), 6.36 (dd, *J* = 8.8, 5.6 Hz, 1H), 5.28 ($t_{app.}$, *J* = 8.8 Hz, 1H), 4.78 ($t_{app.}$, *J* = 8.8 Hz, 1H), 4.38 ($t_{app.}$, *J* = 9.0 Hz, 1H), 3.74 (s, 3H), 2.34 (m_c, 1H), 2.20 (m_c, 1H), 1.37 (m_c, 1H), 1.30-1.10 (m, 5H), 0.86 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7 (C), 159.0 (C), 155.7 (C), 148.6 (CH), 138.6 (C), 136.6 (C), 132.5 (C), 128.93 (CH), 128.89 (CH), 128.7 (CH), 127.6 (CH), 121.1 (CH), 118.4 (CH), 113.1 (CH), 69.7 (CH_2), 59.7 (CH), 54.9 (CH_3), 31.3 (CH_2), 28.8 (CH_2), 27.5 (CH_2), 22.0 (CH_2), 13.6 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{28}NO_4^+$: 394.2013. Found: 394.2011.

(4*S*,5*R*)-3-[(*Z*)-3-(3-Methoxyphenyl)-3-oxo-1-phenylprop-1-en-2-yl]-4,5-diphenyloxazolidin-2-one (11s)

Prepared according to General Method B using ynamide **7i** (577 mg, 1.70 mmol), DCM (15 mL), $Pd(PPh_3)_4$ (98 mg, 0.085 mmol), Bu_3SnH (0.50 mL, 1.79 mmol), 3-methoxybenzoyl chloride (225 µL, 1.60 mmol) and CuTC (32 mg, 0.17 mmol). Flash chromatography (silica gel, 21:79 EtOAc/hexanes) gave the title compound **11s** as a thick gum (610 mg, 75%). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.46-7.38 (m, 5H), 7.30-7.23

(m, 1H), 7.18-7.12 (m, 5H), 7.09-7.00 (m, 4H), 6.99 (s, 1H), 6.92-6.83 (m, 2H), 6.57 (dd, *J* = 8.2, 1.0 Hz, 2H), 5.91 (d, *J* = 8.7 Hz, 1H), 5.57 (d, *J* = 8.7 Hz, 1H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2 (C), 159.4 (C), 156.8 (C), 139.8 (CH), 138.7 (C), 135.1 (C), 133.1 (C), 132.7 (C), 132.4 (C), 129.9 (CH), 129.6 (CH), 129.2 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 127.6 (CH), 126.1 (CH), 122.3 (CH), 119.0 (CH), 113.7 (CH), 80.3 (CH), 65.1 (CH), 55.4 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{26}NO_4^+$: 476.1856. Found: 476.1852.

(*S*,*Z*)-3-[3-(3,5-Dimethoxyphenyl)-1-(4-methoxyphenyl)-3-oxoprop-1-en-2-yl]-4-isopropyloxazolidin-2-one (11t)

Prepared according to General Method B using ynamide **7k** (324 mg, 1.25 mmol), DCM (12 mL), $Pd(PPh_3)_4$ (72 mg, 0.063 mmol), Bu_3SnH (0.37 mL, 1.31 mmol), 3,5-dimethoxybenzoyl chloride (231 mg, 1.15 mmol) and CuTC (24 mg, 0.13 mmol). Flash chromatography (silica gel, 27:73 EtOAc/hexanes) gave the title compound **11t** as a yellow gum (358 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.7 Hz, 2H), 7.32 (s, 1H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 2.3 Hz, 2H), 6.65 (t, *J* = 2.3 Hz, 1H), 4.47 (t, *J* = 8.7 Hz, 1H), 4.21 (dd, *J* = 8.5, 7.3 Hz, 1H), 3.92 (ddd, *J* = 8.8, 7.3, 5.7 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 6H), 1.82 (septet.d, *J* = 6.9, 5.7 Hz, 1H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4 (C), 161.5 (C), 160.6 (C), 157.6 (C), 142.3 (CH), 139.7 (C), 132.4 (CH), 131.3 (C), 125.3 (C), 114.3 (CH), 107.2 (CH), 104.4 (CH), 65.8 (CH_2), 61.4 (CH), 55.6 (CH_3), 55.3 (CH_3), 30.9 (CH), 18.7 (CH_3), 16.8 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{28}NO_6^+$: 426.1911. Found: 426.1913.

(4*S*,5*R*)-5-((3a*S*,6*R*,7a*R*)-8,8-Dimethyl-2,2-dioxidotetrahydro-3H-3a,6-methanobenzo[c]isothiazol-1(4H)-yl)-2,3-dimethyl-4-pentylcyclopent-2-en-1-one (12b)

Prepared according to General Method C using **11b** (5.9 mg, 0.015 mmol) in DCM (1.5 mL) with $MeSO_3H$ (0.1 M in DCM, 1.5 mL, 0.15 mmol), warmed to rt and stirred overnight. Preparative TLC (silica gel, 15:85 EtOAc/hexanes) gave the title compound as an oil (4.7 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (dd, *J* = 7.8, 4.6 Hz, 1H), 3.57 (d, *J* = 3.2 Hz, 1H), 3.23-3.12 (m, 3H), 2.01 (s, 3H), 1.93-1.78 (m, 5H), 1.71 (d, *J* = 0.8 Hz, 3H), 1.54-1.43 (m, 3H), 1.38-1.13 (m, 7H), 1.21 (s, 3H), 0.91 (s, 3H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.4 (C), 171.1 (C), 135.9 (C), 64.8 (CH), 59.0 (CH), 50.1 (CH_2), 49.7 (C), 47.6 (C), 44.9 (CH), 43.5 (CH), 35.0 (CH_2), 32.5 (CH_2), 32.0 (CH_2), 30.5 (CH_2), 26.8 (CH_2), 25.2 (CH_2), 22.5 (CH_2), 20.3 (CH_3), 20.1 (CH_3), 15.2 (CH_3), 14.0 (CH_3), 8.2 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{36}NO_3S^+$: 394.2410. Found: 394.2412.

5-[(3a*S*,6*R*,7a*R*)-8,8-Dimethyl-2,2-dioxidohexahydro-1*H*-3a,6-methanobenzo[*c*]isothiazol-1-yl]-2,3-dimethyl-4-phenylcyclopent-2-enone (12c)

Prepared according to General Method C using **11c** (87 mg, 0.217 mmol) in DCM (2.2 mL) with $MeSO_3H$ (140 µL, 2.17 mmol) and stirred at rt for 24h. The crude product was of good purity (86 mg, 99%), further purification by flash chromatography (silica gel, 6:94 EtOAc/hexanes) gave cleaner product but with significant loss of mass (54 mg, 63%). MP = 102-104 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.2 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 2H), 4.35 (br. s, 1H), 3.89 (dd, *J* = 7.6, 4.8 Hz, 1H), 3.65 (d, *J* = 3.2 Hz, 1H), 3.19 (s, 2H), 1.87 (s, 3H), 1.85-1.80 (m, 4H), 1.78 (m_c, 1H), 1.63 (m_c, 1H), 1.52-1.43 (m, 2H), 1.30-1.20 (m, 2H), 1.11 (s, 3H), 0.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.2 (C), 169.5 (C), 139.8 (C), 136.7 (C), 128.9 (CH), 127.8 (CH), 127.3 (CH), 65.1 (CH), 63.9 (CH), 50.7 (CH), 50.4 (CH_2), 49.9 (C), 47.5 (C), 44.8 (CH), 35.0 (CH_2), 32.3 (CH_2), 26.7 (CH_2), 20.3 (CH_3), 20.0 (CH_3), 15.7 (CH_3), 8.4 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{30}NO_3S^+$: 400.1941. Found: 400.1948.

(*S*)-4-Benzyl-3-[(1*R*,5*S*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-en-1-yl]oxazolidin-2-one (12f)

Prepared according to General Method C using **11f** (50 mg, 0.138 mmol) in DCM (1.4 mL) with $MeSO_3H$ (90 µL, 1.38 mmol), warmed to rt and stirred for 3 d. Trituration with 4:1 hexanes/Et_2O gave the title compound as a white solid (42.5 mg, 85%). X-ray crystal structure obtained from a crystal grown in an evaporating DCM crystallization. MP = 240-242 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (m_c, 2H), 7.30 (m_c, 1H), 7.23-7.13 (m, 5H), 6.87 (m_c, 2H), 4.34-4.16 (m, 3H), 3.97 (dd, *J* = 8.2, 6.7 Hz, 1H), 3.63 (d, *J* = 4.2 Hz, 1H), 2.44 (dd, *J* = 13.8, 4.4 Hz, 1H), 2.32 (dd, *J* = 13.8, 9.1 Hz, 1H), 1.84 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8 (C), 168.5 (C), 157.3 (C), 139.7 (C), 136.0 (C), 135.0 (C), 129.1 (CH), 128.7 (CH), 128.6 (CH), 127.9 (CH), 127.6 (CH), 126.9 (CH), 67.6 (CH_2), 66.4 (CH), 58.5 (CH), 53.0 (CH), 39.7 (CH_2), 15.4 (CH_3), 8.4 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{24}NO_3^+$: 362.1751. Found: 362.1746.

(4*S*,5*R*)-3-((1*R*,5*S*)-3,4-dimethyl-2-oxo-5-pentylcyclopent-3-en-1-yl)-4,5-diphenyloxazolidin-2-one (12h)

Prepared according to General Method C using **11h** (400 mg, 0.959 mmol) in DCM (9.5 mL) with $MeSO_3H$ (621 µL, 9.59 mmol), warmed to rt and stirred for overnight. Flash chromatography (silicagel, 15% EtOAc in hexane) gave the title compound as yellow solid (391.2 mg, 98%). MP = 125.7-127.2. IR: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 – 7.02 (m, 6H), 7.03 – 6.86 (m, 4H), 5.95 (d, *J* = 8.8 Hz, 1H), 5.49 (d, *J* = 8.8 Hz, 1H), 3.41 (d, *J* = 1.2 Hz, 1H), 3.25 (d, *J* = 3.7 Hz, 1H), 1.94 (s, 3H), 1.67 (d, *J* = 1.0 Hz, 3H), 1.46 – 1.21 (m, 3H), 1.11 – 0.90 (m, 4H), 0.74 (t, *J* = 7.1 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.91, 156.77, 140.57, 137.36, 135.80, 135.3, 133.6, 132.9, 132.2, 129.5, 129.4, 128.6, 128.5, 128.2, 128.0, 127.8, 127.6, 126.2, 80.4, 64.9, 14.7, 12.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{27}H_{32}NO_3^+$: 418.2377. Found: 418.2382.

(4*S*,5*R*)-3-((1*R*,5*S*)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-en-1-yl)-4,5-diphenyloxazolidin-2-one (12i)

Prepared according to General Method C using **11i** (200 mg, 0.4728 mmol) in DCM (5 mL) with $MeSO_3H$ (306 μL, 4.728 mmol), warmed to rt and stirred 2 d. Flash chromatography (silicagel, 20% EtOAc in hexane) gave the title compound as clear resin (196 mg, 98%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.15 (m, 3H), 7.09 – 7.02 (m, 3H), 6.96 (dd, *J* = 6.6, 2.9 Hz, 2H), 6.86 (ddd, *J* = 8.6, 6.7, 4.2 Hz, 3H), 6.64 (t, *J* = 7.6 Hz, 2H), 6.41 (d, *J* = 7.2 Hz, 2H), 5.85 (d, *J* = 8.7 Hz, 1H), 5.58 (d, *J* = 8.7 Hz, 1H), 4.64 – 4.55 (m, 1H), 3.36 (d, *J* = 4.4 Hz, 1H), 1.81 (d, *J* = 2.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.0, 169.2, 158.1, 139.8, 136.0, 135.1, 133.1, 129.0, 128.2, 128.1, 128.0, 128.0, 127.9 (2C), 127.5, 126.2, 79.9, 67.8, 66.8, 52.6, 15.6, 8.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{28}H_{26}NO_3^+$: 424.1907. Found: 424.1913.

(4*S*,5*R*)-3-((2*R*,3*S*)-1-Oxo-3-pentyl-2,3,4,5,6,7-hexahydro-1H-inden-2-yl)-4,5-diphenyloxazolidin-2-one (12l)

Prepared according to General Method C using **11l** (87.0 mg, 0.194 mmol) DCM (1.9 mL), $MeSO_3H$ (0.13 mL, 1.94 mmol), at rt for 48 h. Flash chromatography (silica gel, 20:80 EtOAc / hexanes) gave **12l** as pale yellow oil (73.7 mg, 85%). ^1H NMR (401 MHz, $CDCl_3$) δ 7.21 – 7.17 (m, 3H), 7.07 – 7.03 (m, 3H), 6.97-6.95 (m, 2H), 6.90 – 6.82 (m, 3H), 6.64 (t, *J* = 7.6 Hz, 2H), 6.41 (d, *J* = 7.2 Hz, 2H), 5.85 (d, *J* = 8.7 Hz, 1H), 5.57 (d, *J* = 8.7 Hz, 1H), 4.64 (d, *J* = 1.6 Hz, 1H), 3.38 (d, *J* = 4.3 Hz, 1H), 2.39 – 1.90 (m, 4H), 1.74 – 1.57 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.0, 172.4, 185.1, 139.5, 138.0, 135.1, 133.1, 128.9, 128.1, 128.0, 127.9, 127.8, 127.3, 126.1, 79.7, 67.7, 67.1, 51.5, 26.3, 22.2, 21.4, 20.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{27}NO_3^+$: 450.2064, found 450.207.

(4*S*,5*R*)-3-((1*R*,5*S*)-3-(4-methoxyphenyl)-2-oxo-5-phenyl-4-propylcyclopent-3-en-1-yl)-4,5-diphenyloxazolidin-2-one (12m)

Prepared according to General Method C using **11m** (350 mg, 0.644 mmol) in DCM (6 mL) with $MeSO_3H$ (417 μL, 6.44 mmol), heated to 50 ^oC for 2d. Flash chromatography (silicagel, 20% EtOAc in hexane) gave the title compound as an oil (346 mg, 100%, including 7% of the minor *cis*-isomer). ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, *J* = 16.6, 5.3 Hz, 5H), 7.08 (dd, *J* = 6.1, 3.3 Hz, 5H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.92 – 6.85 (m, 3H), 6.67 (t, *J* = 7.6 Hz, 2H), 6.44 (d, *J* = 7.1 Hz, 2H), 5.85 (d, *J* = 8.7 Hz, 1H), 5.61 (d, *J* = 8.6 Hz, 1H), 3.83 (s, 3H), 3.50 (d, *J* = 4.5 Hz, 1H), 2.64 – 2.51 (m, 1H), 2.10 – 1.97 (m, 1H), 1.44 (ddd, *J* = 22.3, 15.8, 7.4 Hz, 2H), 0.80 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.7, 173.4, 159.4, 158.2, 139.9, 139.8, 135.1, 133.1, 130.5, 129.1, 128.3, 128.2, 128.3, 128.2, 127.9, 127.9, 127.5, 126.2, 123.7, 113.9, 79.9, 67.6, 67.2, 55.4, 50.1, 31.3, 20.7, 13.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{36}H_{34}NO_4^+$: 544.2482; Found: 544.2486.

(4*S*,5*R*)-3-((1*R*,5*S*)-3-(4-Methoxyphenyl)-2-oxo-5-pentyl-4-propylcyclopent-3-en-1-yl)-4,5-diphenyloxazolidin-2-one (12n)

Prepared according to General Method C using **11n** (26 mg, 0.048 mmol) in DCM (0.5 mL) with $MeSO_3H$ (32 μL, 0.48 mmol), warmed to rt and stirred 5 d. Flash chromatography (silicagel, 20% EtOAc in hexane) gave the title compound as an oil (24 mg, 92.3%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.04 (m, 8H), 6.95 (ddd, *J* = 22.9, 12.0, 6.3 Hz, 6H), 5.95 (d, *J* = 8.7 Hz, 1H), 5.53 (d, *J* = 8.7 Hz, 1H), 3.81 (s, 3H), 3.58 (dd, *J* = 8.9, 4.8 Hz, 1H), 3.49 (d, *J* = 3.7 Hz, 1H), 2.68 – 2.56 (m, 1H), 2.21 (ddd, *J* = 13.9, 9.0, 5.1 Hz, 1H), 1.50 – 1.39 (m, 3H), 1.17 – 1.06 (m, 4H), 0.91 – 0.81 (m, 7H), 0.78 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.1, 175.3, 159.3, 157.9, 139.8, 135.3, 134.9, 130.5, 128.9, 128.8, 128.2, 128.2, 128.0, 126.1, 123.9, 113.8, 79.6, 67.4, 61.2, 55.4, 42.7, 32.1, 31.0, 29.6, 24.7, 22.4, 21.0, 14.11, 14.08. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{35}H_{40}NO_4^+$: 538.2952; Found: 538.2956.

(*S*)-3-[(1*R*,2*S*,3*R*)-3-Methyl-4-methylene-5-oxo-2-pentyl-3-phenylcyclopentyl]-4-phenyloxazolidin-2-one (12q)

Prepared as a two-step one-pot procedure. Initially the divinyl ketone **11v** was prepared according to General Method B using ynamide **7d** (51.5 mg, 0.20 mmol), DCM (1.3 mL), $Pd(PPh_3)_4$ (12 mg, 0.010 mmol), Bu_3SnH (0.056 mL, 0.21 mmol), (*E*)-2-methyl-3-phenylbut-2-enoyl chloride (41 mg, 0.21 mmol) and CuTC (4.0 mg, 0.010 mmol). The crude product was dissolved in DCM (1.0 mL) and treated with $MeSO_3H$ (32 μL, 0.48 mmol) for 1 h. A solution of $NaHCO_3$ aq. (10% w/v, 3 mL) was added to the reaction mixture, followed by extraction with EtOAc (2 x 10 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (silica gel, 20:80 EtOAc/hexanes) gave the title compound **11p** as a thick gum (37.5 mg, 45% from **7d**). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.42 (s, 5H), 7.32-7.16 (m, 5H), 6.01 (s, 1H), 5.09 (t, *J* = 9.1 Hz, 1H), 4.78 (s, 1H), 4.71 (t, *J* = 8.7 Hz, 1H), 4.27 (t, *J* = 9.2 Hz, 1H), 3.55 (d, *J* = 12.2 Hz, 1H), 3.13 (dt, *J* = 12.2, 6.7 Hz, 1H), 1.31 (s, 3H), 1.27-1.13 (m, 2H), 1.13-0.86 (m, 6H), 0.72 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6 (C), 158.4 (C), 154.7 (C), 146.7 (C), 136.2 (C), 129.5 (CH), 129.0 (CH), 128.7 (CH), 127.9 (CH), 127.4 (CH), 126.4 (CH), 120.6 (CH_2), 70.1 (CH_2), 63.9 (CH), 62.6 (CH), 47.7 (C), 45.9 (CH), 31.7 (CH_2), 28.6 (CH_2), 27.1 (CH_2), 22.1 (CH_2), 20.8 (CH_3), 13.8 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{27}H_{32}NO_3^+$: 418.2377. Found: 418.2389.

(*S*)-3-[(1*S*,2*R*)-5-Methoxy-3-oxo-1-pentyl-2,3-dihydro-1*H*-inden-2-yl]-4-phenyloxazolidin-2-one (12r)

Prepared according to General Method C using **11r** (78.6, 0.2 mmol) in DCM (1.6 mL) with $MeSO_3H$ (32.7 μL, 0.51 mmol), warmed to rt and stirred 3h. Flash chromatography (silica gel, 20/80 EtOAc/hexanes) gave the product **12r** as a clear gum (71 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.37 (m, 5H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.18 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.11 (d, *J* = 2.4 Hz, 1H), 5.20 ($t_{app.}$, *J* = 8.8 Hz, 1H), 4.76 ($t_{app.}$, *J* = 8.8 Hz, 1H), 4.31 ($t_{app.}$, *J* = 9.0 Hz, 1H), 3.81 (s, 3H), 3.80 (m_c, 1H), 3.49 (d, *J* = 5.6 Hz, 1H), 1.64-1.47 (m, 2H), 1.17-0.70 (m, 6H), 0.78 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2 (C), 159.4 (C),

157.8 (C), 147.4 (C), 137.0 (C), 135.9 (C), 129.6 (CH), 129.2 (CH), 128.3 (CH), 125.9 (CH), 124.8 (CH), 104.9 (CH), 70.2 (CH_2), 63.2 (CH), 63.1 (CH), 56.0 (CH_3), 40.7 (CH), 32.0 (CH_2), 30.7 (CH_2), 24.5 (CH_2), 22.3 (CH_2), 14.0 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{28}NO_4^+$: 394.2013. Found: 394.2010.

(4*S*,5*R*)-3-((1*S*,*2R*)-5-methoxy-3-oxo-1-phenyl-2,3-dihydro-1H-inden-2-yl)-4,5-diphenyloxazolidin-2-one (12s)

Prepared according to General Method C using **11s** (800 mg, 1.684 mmol) in DCM (16 mL) with $MeSO_3H$ (327 µL, 5.05 mmol), warmed to rt and stirred 3h. The crude shows mixture of cis and trans products (792 mg, 100%) (used for hydrogenation studies). Then the crude (200 mg) treated with $MeSO_3H$ (10 eq.) gave the *trans* compound (193 mg, 97%). MP = 103.8-105.6 ºC. IR: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 4H), 7.16 (dd, *J* = 8.5, 2.6 Hz, 1H), 7.12 – 7.01 (m, 6H), 6.87 (ddd, *J* = 8.6, 3.9, 1.6 Hz, 3H), 6.65 (d, *J* = 7.6 Hz, 2H), 6.38 (d, *J* = 6.2 Hz, 2H), 5.87 (d, *J* = 8.6 Hz, 1H), 5.67 (d, *J* = 8.6 Hz, 1H), 5.20 (d, *J* = 6.1 Hz, 1H), 3.85 (s, 3H), 3.64 (d, *J* = 6.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.6, 159.9, 158.5, 147.3, 141.0, 135.6, 135.0, 132.7, 128.9, 128.7, 128.2, 128.1, 128.1, 127.9, 127.9, 127.6, 127.5, 126.2, 125.2, 104.8, 80.1, 69.5, 67.8, 55.8, 47.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{26}NO_4^+$: 476.1856. Found: 476.1863.

(*S*)-3-[(2*R*,3*S*)-4,6-Dimethoxy-3-(4-methoxyphenyl)-1-oxo-2,3-dihydro-1*H*-inden-2-yl]-4-isopropyloxazolidin-2-one (12t)

Prepared according to General Method C using **11t** (192 mg, 0.451 mmol) in DCM (9 mL) with $MeSO_3H$ (290 µL, 4.51 mmol), warmed to reflux and stirred overnight. Flash chromatography (silica gel, 10:45:45 Et_2O/DCM/hexanes) gave the title compound **12t** as a discolored solid (155 mg, 81%). MP = 183-185 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 2.2 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 2H), 6.62 (d, *J* = 2.2 Hz, 1H), 4.75 (d, *J* = 4.8 Hz, 1H), 4.38 (t, *J* = 9.0 Hz, 1H), 4.08 (dd, *J* = 8.9, 6.1 Hz, 1H), 3.92 (ddd, *J* = 9.2, 6.1, 3.5 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.74 (d, *J* = 4.8 Hz, 1H), 3.52 (s, 3H), 1.40 (septet.d, *J* = 6.8, 3.5 Hz, 1H), 0.71 (d, *J* = 7.0 Hz, 3H), 0.69 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6 (C), 161.6 (C), 158.3 (C), 158.0 (C), 157.9 (C), 136.7 (C), 136.3 (C), 134.5 (C), 128.4 (CH), 113.7 (CH), 107.2 (CH), 96.1 (CH), 69.4 (CH), 63.6 (CH_2), 62.4 (CH), 55.7 (CH_3), 55.5 (CH_3), 55.2 (CH_3), 46.0 (CH), 28.7 (CH), 17.7 (CH_3), 14.2 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{28}NO_6^+$: 426.1911. Found: 426.1910.

(*S*)-3-{(4S,5*R*)-4-Isopropyl-6-oxo-5,6-dihydro-4H-cyclopenta[b]furan-5-yl}-4-phenyloxazolidin-2-one (12aa)

Triflic acid (45 μL, 0.507 mmol) was added to a stirred solution of **11aa** (66.0 mg, 0.203 mmol) in DCE (4 mL) and the reaction was refluxed for 2 hours. The bath temperature was then lowered to 60°C and the reaction was stirred for a further 16 hours. After this time the reaction was quenched with saturated $NaHCO_3$ and extracted twice with DCM, the combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (silica gel, 30:70 EtOAc/hexanes) gave the title compound as a white solid (16.3 mg, 25%). MP = 137-140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 1.8 Hz, 1H), 7.45-7.33 (m, 5H), 6.46 (d, *J* = 1.8 Hz, 1H), 5.21 ($t_{app.}$, *J* = 8.9 Hz, 1H), 4.73 ($t_{app.}$, *J* = 8.8 Hz, 1H), 4.30 ($t_{app.}$, *J* = 8.9 Hz, 1H), 3.66 (d, *J* = 3.5 Hz, 1H), 3.57 ($t_{app.}$, *J* = 3.8 Hz, 1H), 1.56 (m_c, 1H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.49 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.7 (C), 157.7 (C), 154.6 (C), 153.5 (CH), 152.6 (C), 136.6 (C), 129.7 (CH), 129.2 (CH), 128.3 (CH), 110.4 (CH), 70.0 (CH_2), 64.9 (CH), 62.9 (CH), 44.1 (CH), 28.4 (CH), 21.1 (CH_3), 17.1 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{20}NO_4^+$: 326.1387. Found: 326.1388.

(*S*)-3-((3*S*,4*S*)-3,4-dimethyl-5-oxo-2,3-diphenylcyclopent-1-en-1-yl)-4-isopropyloxazolidin-2-one (23).

$MeSO_3H$ (91 μL, 1.4 mmol) was added to a solution of divinyl ketone **11j** (54 mg, 0.14 mmol) in DCM (1.4 mL) and the reaction stirred at rt for 4 days. A solution of $NaHCO_3$ aq. (10% w/v, 3 mL) was added to the reaction mixture, followed by extraction with EtOAc (2 x 10 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (silica gel, 20:80 EtOAc / hexanes) gave the title compound **23** as a white powder (37.5 mg, 100%). This material recrystallised from chloroform and petroleum spirit by vapour diffusion method to afford a suitable crystal for X-ray crystal structure analysis (above). ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H), 7.25 – 7.18 (m, 3H), 6.98 – 6.94 (m, 2H), 4.24 (t, *J* = 8.8 Hz, 1H), 4.12 (dd, *J* = 8.7, 7.0 Hz, 1H), 3.81 (s, br, 1H), 2.68 (q, *J* = 7.1 Hz, 1H), 1.79 – 1.70 (m, 1H), 1.58 (s, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.71 (d, *J* = 7.1 Hz, 6H). ^{13}C NMR (101MHz, $CDCl_3$) δ 204.31, 156.0, 140.8, 133.9, 133.3, 129.6, 128.8, 128.9, 128.4, 127.7, 127.3, 127.2, 126.5, 64.8, 64.6, 59.051, 54.6, 51.9, 23.5, 18.22, 14.9, 9.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{27}NO_3^+$: 390.2064. Found 390.2068.

(4*S*,5*R*)-3-((1*R*,3*R*,4*S*,5*R*)-3-(4-Methoxyphenyl)-3-(1-methyl-1H-indol-3-yl)-2-oxo-5-phenyl-4-propylcyclopentyl)-4,5-diphenyloxazolidin-2-one (25)

BF_3.THF (30.4 μL, 0.276 mmol) was added to solution of **11m** (150 mg, 0.276 mmol) and *N*-methylindole (362.3 mg, 2.76 mmol) in DCM (2.8 mL) at -78 °C. The reaction mixture was then allowed to warm to RT for 1h. After this time the reaction was quenched with saturated $NaHCO_3$ and extracted twice with DCM (2X10 mL), the combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified using flash chromatography (silica gel, 15% EtOAc in hexane) giving the title compound as a light brown solid (127.2 mg, 77%). MP = 134.2-137.8. IR: ^{1}H NMR (400 MHz, D6-

acetone) δ 7.63 (s, 1H), 7.49 (d, *J* = 7.1 Hz, 2H), 7.42 (t, *J* = 7.3 Hz, 2H), 7.32 (ddd, *J* = 25.2, 16.4, 7.7 Hz, 5H), 7.15 – 7.07 (m, 1H), 7.05 – 6.98 (m, 3H), 6.91 (t, *J* = 7.4 Hz, 1H), 6.83 (ddd, *J* = 10.8, 8.6, 4.2 Hz, 5H), 6.69 (t, *J* = 7.6 Hz, 2H), 6.13 (s, 2H), 5.88 (d, *J* = 8.7 Hz, 1H), 5.38 (d, *J* = 8.7 Hz, 1H), 4.46 (t, *J* = 12.6 Hz, 1H), 3.87 (d, *J* = 13.2 Hz, 1H), 3.79 (d, *J* = 1.0 Hz, 6H), 3.49 – 3.35 (m, 1H), 1.23 – 0.91 (m, 4H), 0.49 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, D6-acetone) δ 212.7, 206.2, 159.6, 159.3, 140.8, 139.2, 136.6, 134.3, 134.2, 131.71, 129.8, 129.6, 129.4, 129.0, 128.5, 128.6, 128.5, 128.4, 128.2, 127.6, 127.1, 124.9, 122.4, 119.2, 116.6, 113.4, 110.0, 80.283, 68.3, 67.4, 60.0, 55.4, 47.4, 47.1, 33.6, 32.9, 22.0, 14.7. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{45}H_{43}N_2O_4^+$: 675.3217. Found: 675.3224.

(4*S*,5*R*)-3-((1*R*,2*S*,a*S*,7a*S*)-3a-(Furan-2-yl)-3-oxo-1-phenyloctahydro-1H-inden-2-yl)-4,5-diphenyloxazolidin-2-one (*trans*-26)

BF_3.THF (0.02 mL, 27.1 mg, 0.1937 mmol)) was added to a stirring solution of divinyl ketone **11l** (87.1 mg, 0.194 mmol), furan (0.28 mL, 263.7 mg, 3.874 mmol) in anhydrous DCM (1.9 mL) at −78 °C, then allowed to slowly warm up to rt for 16 h. Reaction mixture was quenched with $NaHCO_3$ aq. (sat., 3 mL), extracted with DCM (2 x 5mL), washed with water (2 x 5 mL) and brine (2 x 5 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (NEt_3 treated silica gel, 15-25% EtOAc in PS, 10% step gradient) yielded *cis*-**26** as a yellow oil (36.9 mg, 36.8%) and *trans*-**26** as tan oil (38.1 mg, 37.8%). Both isomers were obtained in a combined yield of 75%. *cis*-**26**: ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.32 – 7.27 (m, 3H), 7.25 – 7.22 (m, 2H), 7.07 – 6.98 (m, 3H), 6.94 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.79 (dd, *J* = 7.5, 1.5 Hz, 2H), 6.71 (t, *J* = 6.7 Hz, 2H), 6.36 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.32 (dd, *J* = 3.3, 0.7 Hz, 1H), 6.14 (s, br, 2H), 5.72 (d, *J* = 8.8 Hz, 1H), 5.44 (d, *J* = 8.7 Hz, 1H), 4.48 (t, *J* = 12.3 Hz, 1H), 3.58 (d, *J* = 12.0 Hz, 1H), 2.90 (d, *J* = 12.5 Hz, 1H), 2.16-2.01 (m, 2H), 1.76 – 1.60 (m, 2H), 1.56 – 1.23 (m, 4H).^{13}C NMR (101 MHz, $CDCl_3$) δ 211.0, 158.3, 154.0, 142.0, 138.9, 135.1, 132.73, 129.0, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8. 127.6, 126.2, 110.6, 107.5, 79.6, 68.6, 67.5, 51.4, 42.3, 41.1, 27.0, 22.1, 21.4, 20.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{34}H_{31}NO_4^+$: 518.2326. Found 518.2329. *trans*-**26**: ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.30 – 7.27 (m, 3H), 7.17 (dd, *J* = 6.6, 2.9 Hz, 2H), 7.05 – 6.98 (m, 3H), 6.92 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.78 (dd, *J* = 7.8, 1.3 Hz, 2H), 6.69 (t, *J* = 6.5 Hz, 2H), 6.23 (s, 1H), 6.14 (s, br, 2H), 5.71 (d, *J* = 8.7 Hz, 1H), 5.41 (d, *J* = 8.7 Hz, 1H), 4.44 (t, *J* = 12.2 Hz, 1H), 3.52 (d, *J* = 12.0 Hz, 1H), 2.73 (d, *J* = 12.4 Hz, 1H), 2.15 – 1.95 (m, 2H), 1.66 (d, *J* = 13.0 Hz, 1H), 1.54 – 1.41 (m, 4H), 1.28-1.22 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.6, 158.3, 153.4, 138.8, 135.0, 132.7, 129.0, 128.3, 128.2, 128.1, 128.1, 127.8, 127.6, 126.2, 107.5, 79.6, 68.1, 67.5, 51.3, 42.4, 41.4, 28.1, 22.0, 21.5, 20.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{34}H_{31}NNaO_4^+$: 540.2151. Found 540.2150.

(4*S*,5*R*)-3-((1*R*,3*S*,4*S*,5*R*)-3-(Furan-2-yl)-2-oxo-4,5-diphenylcyclopentyl)-4,5-diphenyloxazolidin-2-one (27)

BF_3.THF (0.02 mL, 0.197 mmol) was added to a solution of **11o** (92.9mg, 0.1970mmol) and furan (0.29 mL, 3.94 mmol) and in anhydrous DCM (2.0 mL) at −78°C, then the reaction allowed to warm to rt and stir for 2 h. To this $NaHCO_3$ aq. (sat., 2.0 mL) was added and the mixture extracted with DCM (2 x 4mL), washed with water (2 x 4mL) and brine (2 x 4 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (silica gel, 20% EtOAc / hexanes) gave **27** as pink oil (69.5 mg, 65%). ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.21 – 7.11 (m, 10H), 7.08 – 6.99 (m, 3H), 6.96 (tt, *J* = 7.4, 1.0 Hz, 1H), 6.81 (dd, *J* = 7.6, 1.4 Hz, 2H), 6.71 (t, *J* = 8.0 Hz, 1H), 6.26 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.18-6.10 (m, 3H), 5.76 (d, *J* = 8.6 Hz, 1H), 5.55 (d, *J* = 8.6 Hz, 1H), 4.60 (t, *J* = 11.9 Hz, 1H), 3.93 (d, *J* = 11.9 Hz, 1H), 3.72 (t, *J* = 11.9 Hz, 1H), 3.68 (dd, *J* = 11.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 158.9, 149.1, 142.5, 138.8, 138.1, 134.8, 132.4, 128.8, 128.6, 128.3, 128.3, 128.1, 128.0, 127.8, 127.7, 127.5, 127.3, 126.2, 110.6, 109.1, 80.0, 68.0, 67.7, 55.7, 49.9, 48.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{36}H_{30}NO_4^+$: 540.2169. Found 540.2172.

(4*S*,5*R*)-3-((1*S*,3*R*,4*S*,5*R*)-3-(4-Methoxyphenyl)-3-methyl-2-oxo-5-phenyl-4-propylcyclopentyl)-4,5-diphenyloxazolidin-2-one (28)

To a solution of **11m** (50 mg, 0.092 mmol) in DCM (0.9 mL, 0.1M) with activated 4Å MS (100 mg) was added 2.5 equivalents of $AlMe_3$ (.115 mL, 2.0 M solution in toluene) at −78 ˚C. The reaction mixture was warmed to room temperature and stirred for overnight. The reaction was quenched with 2M aq. HCl (1 mL) at 0 ^{o}C and warmed to room temperature. After separation of the phases, the aqueous layer was extracted with DCM (3 x 5 mL). The combined organic extracts were washed with brine, and dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash column chromatography (silica gel, 20:80 EtOAc / hexanes) provided the desired product **28** (18 mg, 35 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.15 (m, 7H), 7.09 – 6.90 (m, 5H), 6.85 (d, *J* = 8.9 Hz, 2H), 6.80 – 6.65 (m, 4H), 6.10 (s, 1H), 5.69 (d, *J* = 8.7 Hz, 1H), 5.45 (d, *J* = 8.8 Hz, 1H), 4.11 (t, *J* = 12.0 Hz, 1H), 3.78 (s, 3H), 3.57 (d, *J* = 12.3 Hz, 1H), 2.68 – 2.53 (m, 1H), 1.51 (s, 3H), 1.47 – 1.24 (m, 2H), 0.95 – 0.80 (m, 1H), 0.71 (ddd, *J* = 19.7, 12.8, 7.5 Hz, 1H), 0.55 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.9, 158.4, 158.3, 140.1, 136.0, 135.1, 132.7, 128.9, 128.4, 128.3, 128.1, 128.0, 128.0, 127.929, 127.8, 127.5, 126.2, 113.9, 79.7, 69.4, 67.4, 55.4, 54.3, 49.3, 46.8, 31.3, 21.4, 17.0, 14.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{37}H_{38}NO_4^+$: 560.2795. Found: 560.2793.

(4*S*,5*R*)-3-((4a*R*,9S,10*R*,10a*S*)-6,7-Dimethyl-11-oxo-10-phenyl-1,2,3,4,5,8,10,10a-octahydro-9H-4a,9-methanobenzo[8]annulen-9-yl)-4,5-diphenyloxazolidin-2-one (29)

BF_3.THF (0.03 mL, 39.6 mg, 0.2834 mmol) was added to a stirring solution of **11l** (127.4 mg, 0.2834 mmol) and 2,3-dimethyl-1,3-butadiene (0.64 mL, 465.6 mg, 5.668 mmol) in anhydrous DCM (2.8 mL) at −10 °C. The reaction mixture was at −10 °C for 1.5 h, whereupon TLC revealed that **11j** was fully consumed. The reaction was then quenched with saturated $NaHCO_3$ (3mL), extract with DCM (2 x 5 mL), washed with

water (2 x 5 mL) and brine (2 x 5 mL), dried over $MgSO_4$ and concentrated. Flash chromatography (treated silica gel pretreated with 1% Et_3N, 1:9 EtOAc / hexanes) gave product as white solid (48.2 mg, 32%). MP = 187-9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.19-7.14 (m, 5H), 7.05-7.03 (m, 3H), 6.91-6.88 (m, 2H), 6.82 (tt, *J* = 7.4, 1.1Hz, 1H), 6.65 (t, *J* = 7.4 Hz, 2H), 6.41 (d, *J* = 7.3 Hz, 2H), 5.87 (d, *J* = 8.7 Hz, 1H), 5.36 (d, *J* = 8.8 Hz, 1H), 4.58 (dd, *J* = 10.9, 1.3 Hz, 1H), 2.37 (dt, *J* = 11.4, 5.8 Hz, 1H), 2.26 (q, *J* = 17.1Hz, 2H), 2.08 (d, *J* =17.1Hz, 1H), 2.02-1.94 (m, 1H), 1.80-1.70 (m, 3H), 1.66 (s, 3H), 1.60-1.46 (m, 3H), 1.42-1.32 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 219.6, 158.6, 138.7, 136.6, 135.4, 130.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.4, 127.2, 126.3, 126.2, 123.8, 79.5, 74.1, 65.2, 49.8, 49.0, 47.2, 41.6, 40.3, 26.8, 23.5, 23.0, 22.9, 17.2, 16.8. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{36}H_{37}NO_3$ $(M+H)^+$: 532.2846. Found 532.2855.

(4*S*,5*R*)-3-[(1*Z*,4*E*)-6-(3-methoxyphenoxy)-4-methyl-3-oxo-1-phenylhexa-1,4-dien-2-yl]-4,5-diphenyloxazolidin-2-one (30)

Prepared according to General Method B using ynamide **7i** (982 mg, 2.89 mmol), DCM (29 mL), $Pd(PPh_3)_4$ (100 mg, 0.087 mmol), Bu_3SnH (0.82 mL, 3.04 mmol), (*E*)-4-(3-methoxyphenoxy)-2-methylbut-2-enoyl chloride[12] (708 mg, 2.74 mmol) and CuTC (55 mg, 0.29 mmol). Flash chromatography (silica gel, 22:78 EtOAc/hexanes) gave the title compound as a white solid (1.20 g, 76%). MP = 59-62 °C. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.43-7.38 (m, 3H), 7.35-7.28 (m, 2H), 7.15-7.10 (m, 4H), 7.01-6.94 (m, 3H), 6.93 (s, 1H), 6.83 (t, *J* = 7.7 Hz, 2H), 6.55-6.46 (m, 3H), 6.42 (ddd, *J* = 8.1, 2.3, 0.6 Hz, 1H), 6.39 (t, *J* = 2.3 Hz, 1H), 6.27 (td, *J* = 5.7, 1.2 Hz, 1H), 5.85 (d, *J* = 8.7 Hz, 1H), 5.43 (d, *J* = 8.7 Hz, 1H), 4.72 (ddq, *J* = 14.3, 5.9, 0.8 Hz, 1H), 4.59 (ddq, *J* = 14.3, 5.1, 1.0 Hz, 1H), 3.73 (s, 3H), 1.94 (q, *J* = 1.0, Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.1 (C), 160.8 (C), 159.3 (C), 156.6 (C), 138.5 (CH), 137.6 (CH), 137.5 (C), 135.0 (C), 133.1 (C), 132.6 (C), 131.7 (C), 129.9 (CH), 129.6 (CH), 129.5 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.7 (CH), 127.5 (CH), 126.1 (CH), 106.8 (CH), 106.7 (CH), 101.3 (CH), 80.3 (CH), 64.9 (CH), 64.7 (CH_2), 55.2 (CH_3), 13.4 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{35}H_{32}NO_5^+$: 546.2275. Found: 546.2280.

(4*S*,5*R*)-3-{(2*R*,3*R*,3a*S*,9b*R*)-7-Methoxy-9b-methyl-1-oxo-3-phenyl-1,2,3,3a,4,9b-hexahydrocyclopenta[*c*]chromen-2-yl}-4,5-diphenyloxazolidin-2-one (31)

BF_3.THF (101 µL, 0.917 mmol) was added to a solution of **30** (500 mg, 0.917 mmol) in toluene (9 mL) with stirred at 0 °C for 1 h. The reaction was then quenched with saturated $NaHCO_3$ (20 mL), extract with EtOAc (2 x 15 mL), washed with water (2 x 10 mL) and brine (2 x 10 mL), dried over $MgSO_4$ and concentrated. Flash chromatography (silica gel, 8:46:46 Et_2O/DCM/hexanes) gave the title compound as a yellow gum (440 mg, 88% including 5% of the minor *cis*-isomer). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.43-7.27 (m, 5H), 7.20 (d, *J* = 8.8 Hz, 1H), 7.04-6.94 (m, 3H), 6.82 (tt, *J* = 7.5, 1.2 Hz, 1H), 6.80-6.73 (m, 2H), 6.66 (t, *J* = 7.3 Hz, 2H), 6.40 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.33 (br. s., 2H), 6.24 (d, *J* = 2.5 Hz, 1H), 5.56 (d, *J* = 8.7 Hz, 1H), 5.09

(d, *J* = 8.7 Hz, 1H), 4.33 (d, *J* = 13.2 Hz, 1H), 3.99 (dd, *J* = 11.6, 1.9 Hz, 1H), 3.86-3.76 (m, 2H), 3.74 (s, 3H), 2.10 (dt, *J* = 11.6, 1.9 Hz, 1H), 1.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.9 (C), 159.5 (C), 158.2 (C), 154.0 (C), 137.6 (C), 134.7 (C), 132.3 (C), 129.7 (CH), 129.2 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.8 (CH), 127.7 (CH), 127.61 (CH), 127.59 (CH), 125.9 (CH), 112.6 (C), 109.2 (CH), 101.5 (CH), 79.4 (CH), 65.5 (CH), 65.0 (CH), 60.7 (CH_2), 55.1 (CH_3), 47.2 (CH), 45.7 (C), 41.7 (CH), 27.0 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{35}H_{32}NO_5^+$: 546.2275. Found: 546.2282.

(*R*)-6-methoxy-3-pentyl-2,3-dihydro-1*H*-inden-1-one (34)

Prepared according to General Method D using **12r** (113 mg, 0.35 mmol) in THF (4 mL) using lithium naphthalenide in THF (~ 1.0 M, 0.8 mL). Flash chromatography (silica gel, 5% EtAcO in hexane) as a clear oil (74 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.31 Hz, 1H), 7.38-7.36 (m, 1H), 3.79 (s, 3H), 3.24-3.21 (m, 1H), 2.85 (dd, *J* = 18.3, 6.7 Hz 1H), 2.36 (dd, *J* =18.3, 2.3 Hz 1H), 1.90-1.86 (m 1H), 1.44-1.18 (m, 8H), 0.8 (m, 3H). ^{13}C NMR δ 205.2 (C), 158.8 (C), 150.2 (C), 137.6 (C), 127.0 (CH), 123.2 (CH), 108.1 (CH), 56.6 (CH_3), 45.6 (CH), 38.1 (CH), 36.0 (CH_2), 31.8 (CH_2), 26.1 (CH_2), 21.8 (CH), 13.4 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_{21}O_2^+$: 233.1542. Found: 233.1546 Optical rotation: T = 22.78 °C, $[\alpha]_D$ = - 0.03 (c = 24.8, MeOH).

(3*R*,3a*S*,9b*R*)-7-Methoxy-9b-methyl-3-phenyl-2,3,3a,4-tetrahydrocyclopenta[*c*]chromen-1(9b*H*)-one (37)

Prepared according to General Method D using **31** (87.1 mg, 0.200 mmol), THF (4 mL) and lithium naphthalenide (~0.89 M, 0.46 mL, 0.41 mmol). Flash chromatography (silica gel, 6:47:47 Et_2O/DCM/hexanes) gave the title compound as a white solid (56.4 mg, 91%). MP = 92-95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.26 (m, 6H), 6.55 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.44 (d, *J* = 2.6 Hz, 1H), 4.12 (dd, *J* = 11.4, 1.9 Hz, 1H), 3.99 (dd, *J* = 11.4, 2.0 Hz, 1H), 3.78 (s, 3H), 3.42 (td, *J* = 11.6, 8.6 Hz, 1H), 2.79 (dd, *J* = 19.1, 8.6 Hz, 1H), 2.55 (dd, *J* = 19.1, 12.0 Hz, 1H), 2.23 (dt, *J* = 11.4, 1.9 Hz, 1H), 1.52 (s, 3H). The spectral data of this material are identical to that previously reported.[10]

***tert*-Butyl ((1*R*,5*S*)-3,4-dimethyl-2-oxo-5-pentylcyclopent-3-en-1-yl)carbamate (39)**

Prepared according to General Method E using **12h** (50 mg, 0.12 mmol), THF (4 mL), Pd/C (10%) (50 mg) and and Boc anhydride (157 mg, 0.72 mmol). Flash chromatography (silicagel, 10% EtOAc in hexanes) gave the title compound **39** as a tan oil (27 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 (d, *J* = 5.5 Hz, 1H), 3.55 – 3.38 (m, 1H), 2.54 – 2.31 (m, 2H), 2.05 (ddd, *J* = 15.5, 10.4, 5.2 Hz, 1H), 1.70 – 1.55 (m, 1H), 1.43 (s, 9H), 1.31 (dd, *J* = 8.7, 3.9 Hz, 6H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.89 (t, *J* = 6.6 Hz, 3H), 0.77 (d, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 217.6, 155.8, 80.1, 60.6, 48.0, 44.3, 32.8, 32.1, 28.9, 28.4, 27.0,

22.7, 14.2, 10.0, 9.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{32}NO_3^+$: 298.2377. Found: 298.2368. $[\alpha]_D$ -44.19 (c = 1, DCM)

(1*S*,2*R*,3*R*,4*R*,5*R*)-2-(Diethylamino)-4,5-dimethyl-3-phenylcyclopentan-1-ol (41)

Prepared according to General Method E using **12i** (50 mg, 0.118 mmol), (4 mL), Pd/C (10%) (50 mg) and acetaldehyde (52.1 mg, 1.18 mmol). After filtration through Celite the combined organic phases were concentrated under reduced pressure. The crude residue was dissolved in methanol (2 mL), $NaBH_4$ (25 mg, 0.6608 mmol) added and the reaction mixture stirred at rt for 6 h. The reaction mixture was then diluted with H_2O (8 mL) and extracted into EtOAc (2 x 5 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude was chromatographed (silicagel, 10% EtOAc in Hexane) gave the title compound **41** as clear oil (24.1 mg, 78%). ^{1}H NMR (400 MHz, D6-acetone) δ 7.38 – 7.12 (m, 5H), 3.77 (dd, *J* = 10.5, 7.6 Hz, 1H), 3.70 – 3.58 (m, 1H), 3.51 (dd, *J* = 10.5, 7.5 Hz, 1H), 2.83 (s, 1H), 2.74 – 2.43 (m, 4H), 2.25 (dq, *J* = 14.6, 7.2 Hz, 1H), 2.00 (dt, *J* = 12.9, 6.6 Hz, 1H), 1.04 (d, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 6H), 0.50 (d, *J* = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, D6-acetone) δ 143.04, 129.63, 128.9, 126.8, 76.1, 65.8, 51.3, 46.7, 45.7, 40.9, 14.9, 13.7, 12.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{27}NO^+$: 261.2087. Found: 261.2051. $[\alpha]_D$: +42.25 (c = 1, DCM).

***tert*-Butyl ((1*R*,3*R*,4*S*,5*R*)-3-(4-methoxyphenyl)-3-(1-methyl-1H-indol-3-yl)-2-oxo-5-phenyl-4-propylcyclopentyl)carbamate (42)**

Prepared according to General Method E using **28** (45 mg, 0.0667 mmol), EtOAc (2 mL), Pd/C (10%) (45 mg) and Boc anhydride (87.42 mg, 0.4 mmol). Flash chromatography (silica gel, 20:80 EtOAc/hexanes) gave the title compound **42** as yellow oil (18.9 mg, 52%). ^{1}H NMR (400 MHz, D6-acetone) δ 7.53 (s,1H), 7.35 (d, *J* = 7.4 Hz, 2H), 7.28 – 7.09 (m, 5H), 6.96 (t, *J* = 7.1 Hz, 3H), 6.67 (t, *J* = 8.9 Hz, 2H), 6.31 (d, *J* = 8.5 Hz, 1H), 4.67 – 4.44 (m, 1H), 3.75 (s, 3H), 3.64 (s, 3H), 3.23 (d, *J* = 7.9 Hz, 2H), 1.15 (s, 9H), 1.05 – 0.94 (m, 2H), 0.92 – 0.82 (m, 2H), 0.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, D6-acetone) δ 213.5, 206.3, 159.2, 156.6, 141.5, 139.3, 134.2, 131.7, 129.5, 129.3, 129.2, 127.8, 127.8, 124.81, 122.3, 119.1, 117.1, 113.4, 109.9, 78.9, 64.4, 60.4, 55.4, 51.1, 48.7, 33.5, 323.0, 28.2, 22.0, 14.7. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{35}H_{41}N_2O_4^+$: 553.3066. Found: 553.3059. $[\alpha]_D$ +24.3 (c = 1, DCM)

***tert*-Butyl((2*R*,3*R*,3a*S*,9b*R*)-7-methoxy-9b-methyl-1-oxo-3-phenyl-1,2,3,3a,4,9b-hexahydrocyclopenta[c]chromen-2-yl)carbamate (43)**

Prepared according to General Method E using **31** (200 mg, 0.3668 mmol), THF (10 mL), Pd/C (10%) (200 mg) and Boc anhydride (480 mg, 2.197 mmol). Flash chromatography (silica gel, 20:80 EtOAc in hexanes) gave the product **43** as a white solid (93 mg, 60%). MP = 79.4-83.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50

(d, *J* = 8.8 Hz, 1H), 7.42 – 7.27 (m, 5H), 6.56 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.39 (d, *J* = 2.6 Hz, 1H), 4.74 (s, 1H), 4.50 (s, 1H), 4.09 (d, *J* = 10.5 Hz, 1H), 3.92 (dd, *J* = 11.5, 2.0 Hz, 1H), 3.76 (s, 3H), 3.07 (t, *J* = 12.2 Hz, 1H), 2.20 (d, *J* = 11.7 Hz, 1H), 1.57 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.6, 159.9, 155.7, 154.7, 137.7, 130.4, 128.9, 128.1, 127.6, 113.4, 109.2, 101.9, 80.1, 61.1, 55.4, 47.0, 46.8, 45.5, 28.2, 27.1. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{29}NNaO_5^+$: 446.1938. Found: 446.1945. $[\alpha]_D$ +23.5 (c = 1, DCM)

***tert*-Butyl [(1*S*,2*R*,3*S*)-3-hydroxy-5-methoxy-1-phenyl-2,3-dihydro-1*H*-inden-2-yl]carbamate (44)**

Prepared according to General Method E using **12s** (68 mg, 0.143 mmol) EtOAc (2 mL), Pd/C (10%) (68 mg) and Boc anhydride (131 mg, 0.6 mmol). Flash chromatography (silicagel, 20:80 EtOAc /hexanes) gave the title compound **44** as clear oil (30.5 mg, 76%). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.42-7.29 (m, 3H), 7.26 (d, *J* = 7.3 Hz, 2H), 7.04 (d, *J* = 2.1 Hz, 1H), 6.77 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 5.24 (br. s., 1H), 5.15 (d, *J* = 6.2 Hz, 1H), 5.01 (br. s., 1H), 3.97 (ddd, *J* = 9.5, 6.2, 2.8 Hz, 1H), 3.91 (d, *J* = 9.5 Hz, 1H), 3.83 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9 (C), 133.3 (C), 128.9 (CH), 128.6 (CH), 127.6 (CH), 125.2 (CH), 115.5 (CH), 108.1 (CH), 80.7 (C), 80.0 (CH), 70.7 (CH), 55.5 (CH_3), 53.3 (CH), 28.3 (CH_3). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{16}NO_3^+$: 282.1125. Found: 282.1110. $[\alpha]_D$ +8.1 (c = 1, DCM)

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Supporting Information

X-ray crystal structure data and CIF files for **12c** and **23**. Copies of ^{1}H NMR and ^{13}C NMR spectra for all new compounds. Chiral HPLC data and 2D NMR data on **27**, **29** and **41**. Details of computational methods, and computational data.

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