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Enantioselective Synthesis of 5,7-Bicyclic Ring Systems from Axially Chiral Allenes Using a Rh(I)-Catalyzed Cyclocarbonylation Reaction

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Abstract

A transfer of chirality in an intramolecular Rh(I)-catalyzed allenic Pauson-Khand reaction (APKR) to access tetrahydroazulenones, tetrahydrocyclopenta[*c*]azepinones and dihydrocyclopenta[*c*]oxepinones enantioselectively (22 – 99% ee) is described. The substitution pattern of the allene affected the transfer of chiral information. Complete transfer of chirality was obtained for all trisubstituted allenenes, but loss of chiral information was observed for disubstituted allenenes. This work constitutes the first demonstration of a transfer of chiral information from an allene to the 5-position of a cyclopentenone using a cyclocarbonylation reaction. The absolute configuration of the corresponding cyclocarbonylation product was also established, something that is rarely done.

Introduction

Cyclopentanes serve as valuable building blocks in organic synthesis and are present in many naturally occurring compounds. Among the various polycyclic skeletons possessing five-membered carbocycles, the fused 5,5-, 5,6- and 5,7-bicyclic ring systems are common structural features found in many biologically relevant compounds.¹ For many natural products, the five-membered rings are characterized by a relatively high oxidation state (Figure 1). Swartzianin D (**1**) is an excellent example of this, where every carbon of the five-membered ring is occupied with a double bond, a carbonyl or a hydroxyl group.² There are a number of synthetic methods available to prepare these highly oxidized rings, but the options narrow rapidly when constructing five-membered carbocycles with stereogenic centers enantioselectively.³

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Supporting Information Copies of ¹H and ¹³C NMR spectra for all new compounds; HPLC chromatogram of the racemic and enantioenriched compounds; coordinates for the crystallographic analysis (CIF) for compounds **35c** and **48**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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There is a diverse array of methods to create stereogenic centers of cyclopentanes in a stereoselective manner. A common synthetic strategy is to take advantage of the chiral pool as a source of enantiopure materials. One example is the asymmetric synthesis of (+)-chinensiolid B (**2**), where the cyclopentane moiety of this compound is generated via a Favorskii rearrangement of (*R*)-carvone.⁴ Moreover, the cyclopentane ring of tecomanine (**3**), possessing a tetrahydrocyclopentapyridinone ring system, was also prepared from (–)-carvone.⁵ Other approaches to install stereogenic centers utilize existing stereocenters on rings adjacent to the five-membered carbocycle. For instance, the methyl group located at the C4 position of grosshemin (**4**) was installed by classic alkylation of an enol acetate of a 5,7-bicyclic ring system to yield a single product diastereoselectively.⁶ However, this diastereoselective approach is not always reliable for cyclopentenone-containing 5,7-ring systems. For example, in the synthesis of (+)-achalensiolid (**5**), reduction of the C1-C11 double bond of a dienone group via a hydrogenation reaction afforded a 1:1 mixture of diastereomers.⁷ In some cases, asymmetric reactions are used to introduce stereogenic atoms but in less direct ways. For example, the five-membered carbocycle of arglabin (**6**) was obtained via an enantioselective cyclopropanation of a furan followed by a rearrangement to produce a protected hydroxy-2-cyclopentenone.⁸ The key stereodetermining step for C4 and C5 stereocenters of connatusin B (**7**) were established using a Diels-Alder reaction starting with cyclopentenone and enantiomerically pure *cis*-1,2-dihydrocatechol.⁹

Other synthetic methods implemented for the preparation of chiral non-racemic 2-cyclopentenones are the Nazarov cyclization and the Pauson-Khand reaction (PKR). The asymmetric Nazarov cyclization has been made possible by the use of chiral auxiliaries, chiral Lewis acids and transfer of axial to tetrahedral chirality when using allenes.¹⁰ However, the electrocyclization process requires an enantioselective formation of the stereogenic carbon beta to the carbonyl controlled by torquoselectivity, followed by a diastereoselective addition of an electrophile to the intermediate enol to form a second stereogenic center adjacent to the newly formed carbonyl.¹¹ The asymmetric PKR has been performed using chiral metal complexes of rhodium,¹² titanium,¹³ iridium¹⁴ and cobalt¹⁵ to provide cyclopentenone-containing bicyclic ring systems in good enantioselectivities. Nevertheless, like the Nazarov cyclization, all reactions establish a stereogenic carbon beta to the carbonyl. There are exceptions for both intra- and intermolecular PKRs where a stereocenter adjacent to the carbonyl is set. These reactions typically involve functionalization of the alkene component with a chiral auxiliary and for nearly all cases this chiral auxiliary is removed and the stereogenic center is lost.¹⁶ While there are methods to synthesize 2-cyclopentenones possessing a stereogenic center at the C5 position stereoselectively, the scope of these protocols is limited.¹⁷

Previously, we demonstrated that a complete transfer of chirality is obtained for chiral, non-racemic allenes **10** in the molybdenum- or zirconium-mediated PKR to afford 2-cyclopentenones **11** enantioselectively (Scheme 1).¹⁸ For both of these transformations, the reaction occurs with the proximal double bond of the allene to provide *E*- α -alkylidene or *E*- α -silylidene 2-cyclopentenones with the stereogenic center beta to the carbonyl group.¹⁹ Since a general protocol for the asymmetric synthesis of C5-substituted bicyclic cyclopentenones is valuable, we considered employing chiral allenes in a PKR to gain access to this motif. Based on these prior results, we envisioned that transfer of chiral information from allene **10** to a stereogenic center adjacent to the carbonyl group of 2-cyclopentenone **12** should also be possible for the Rh(I)-catalyzed cyclocarbonylation reaction, a transformation performed by the selective reaction with the distal π -bond of allene **10** (Scheme 1). Herein are reported studies directed toward a Rh(I)-catalyzed allenic Pauson-Khand reaction (APKR) to afford 5,7-bicyclic ring systems enantioselectively.

Results and Discussion

Investigations into the scope and limitations of the transfer of allene axial chirality in the Rh(I)-catalyzed cyclocarbonylation reaction began with the synthesis of a series of enantiomerically enriched allene-ynes. The substitution pattern of the allene was varied to include trisubstituted allenylsilane **13**, trisubstituted non-silylated allenes **14** – **16** and disubstituted allenes **17** – **19** (Figure 2). The terminus of the alkyne was substituted with either hydrogen, alkyl, aryl, heterocyclic or silyl groups (R^3 = H, Me, cyclopropyl, Ph, 2- and 3-thiophene and TMS) and three different tethers were prepared, two heteroatom-containing (X = NTs, O) and one all carbon-containing (X = C(CO₂Et)₂).

Synthesis of enantiomerically enriched allenes

Synthesis of trisubstituted chiral allenyl alcohol (R_a)-**22** was performed in four steps starting from commercially available ($\pm$)-3-butyne-2-ol (**20**) in a manner analogous to that reported by Brawn and Panek (Scheme 2, eq 1).²⁰ Addition of *n*-butyllithium to alkyne **20** in the presence of lithium chloride followed by addition of phenyldimethylchlorosilane afforded silylated alkyne **21** in 90% yield. Kinetic resolution of racemic propargyl alcohol **21** using lipase AK “Amano” provided enantioenriched propargyl alcohol (*S*)-**21** (47% yield, >98% ee) and the corresponding propargyl acetate (43% yield, >99% ee, not shown). Enantioenriched propargyl alcohol (*S*)-**21** was reacted with trimethylorthoacetate and propionic acid to produce the corresponding allenyl ester via a Johnson-Claisen rearrangement. The methyl ester was reduced with lithium borohydride to afford enantioenriched allenylsilane (R_a)-**22** in >93% ee. The enantiomeric excess was determined by chiral HPLC analysis. Synthesis of racemic allenyl alcohol **25** involved silylation of hept-2-yn-1-ol (**23**) followed by a retro-Brook rearrangement to afford propargyl alcohol **24** in 55% yield for the two steps (Scheme 2, eq 2). A Johnson-Claisen rearrangement performed on alcohol **24** followed by reduction of the methyl ester with lithium aluminum hydride provided allene **25**. Disubstituted allene (R_a)-**26** was prepared by a Johnson-Claisen rearrangement of commercially available (*R*)-3-butyne-2-ol (**20**) followed by lithium aluminum hydride reduction of the corresponding methyl ester (Scheme 2, eq 3). The enantiomeric excess of (R_a)-**26** was based upon chiral HPLC analysis of *p*-nitrobenzoyl ester **27**, for which a >99% ee was obtained. Allenyl alcohol (R_a)-**29** was prepared from 1-hexyne by a palladium-catalyzed carbonylation reaction followed by reduction of the corresponding ynone carbonyl with (*R*)-alpine borane (Scheme 2, eq 4).²¹ The resulting propargyl alcohol (*R*)-**28** was converted into a propargyl vinyl ether with ethyl vinyl ether and mercury acetate. A gold(I)-catalyzed [3,3]-sigmatropic rearrangement of the vinyl ether followed by *in situ* reduction of the intermediate aldehyde afforded allenyl alcohol (R_a)-**29** in >79% ee.²² The enantiomeric excess was determined by chiral HPLC analysis.

Preparation of the Allenic Pauson-Khand Precursors

Allene-ynes **13a** – **13e**, **13g**, **14c** – **14e**, **14g**, **17c**, **17d** and **17f** were all prepared using a Mitsunobu reaction of the corresponding allenols and the appropriately substituted propargyl tosylamides **30a** – **30g** (Scheme 3). Reacting (R_a)-**22** with 3- and 2-thiophene-substituted propargyl tosylamides **30a** and **30b** gave allene-ynes **13a** and **13b** in 90% and 70% yield, respectively. Similarly, high yields were obtained for the Mitsunobu reaction between (R_a)-**22** and **30c**, **30d**, **30e** and **30g** giving **13c**, **13d**, **13e** and **13g** in 92%, 92%, 90% and 73% yield, respectively. Allene-ynes **14c**, **14d**, **14e** and **14g** were obtained in a similar manner in high yields (77% – 93%) from the reaction of trisubstituted allene (R_a)-**29** and propargyl tosylamides **30c**, **30d**, **30e** and **30g**, respectively. Reacting (R_a)-**26** with propargyl tosylamides **30c**, **30d** and **30e** afforded **17c**, **17d** and **17e** in 74%, 85% and 84% yield, respectively. The trimethylsilyl-substituted alkynes **13f**, **14f** and **17f** were prepared by deprotonation of allene-ynes **13e**, **14e** and **17e** with lithium hexamethyldisilylazide followed

by addition of trimethylsilyl chloride to provide the corresponding silylated alkynes in 87%, 80% and 84% yield, respectively.

Allene-ynes **15c**, **15d**, **15f** and **18c**, **18d**, **18f** containing an oxygen atom in the tether were synthesized by a Williamson etherification reaction (Scheme 4). Reacting (*R_a*)-**26** with propargyl bromides **31c**, **31d** and **31e** afforded allene-ynes **18c**, **18d** and **18e** in 83%, 63% and 41% yield, respectively. Reacting (*R_a*)-**29** with propargyl bromides **31c**, **31d** and **31e** produced ethers **15c**, **15d** and **15e** in 27%, 35% and 20% yield, respectively. Low yields for this series of compounds were attributed to the sterically congested environment at the proximal double bond of the allene. This hypothesis is supported by the complete recovery of starting material for the reaction of trisubstituted allenyl alcohol (*R_a*)-**22** with **31d**. The trimethylsilyl-substituted alkynes **15f** and **18f** were prepared by deprotonation of allene-ynes **15e** and **18e** using the same conditions as for allene-ynes **13f**, **14f** and **17f** to provide the corresponding silylated alkynes in 65% and 69% yield, respectively.

Preparation of allene-ynes **16c** – **16e** was accomplished by reaction of alcohol (*R_a*)-**26** with methanesulfonyl chloride to produce mesylate **32**. Addition of the mesylate to the sodium salt of malonates **34c** – **34e** provided the desired allene-ynes in 42 – 75% yields (Scheme 5). Allene-ynes **19c** – **19e** were obtained in an analogous manner from alcohol (*R_a*)-**29** with yields ranging from 57% to 63%. Reaction of **16e** and **19e** with lithium hexamethyldisilylazide and trimethylsilylchloride afforded allene-ynes **16f** and **19f** in 84% and 80% yield, respectively. Attempts to convert alcohol (*R_a*)-**22** to the corresponding allene-ynes using these conditions resulted in an inseparable mixture of silylated and desilylated products. For this reason, the silylated allene series of compounds bearing the oxygen tether was not further pursued.

Optimization of the Cyclocarbonylation Reaction

A brief examination of the cyclocarbonylation reaction conditions was performed using **13c** and it was shown that the standard conditions developed in our group for the Rh(I)-catalyzed APKR provided compound **35** in 95% yield (Scheme 6 and Table 1, entry 1). Attempts to lower the catalyst loading to 5 mol % decreased the yield of the cyclocarbonylation product **35** to 75% and resulted in a 9% yield of cross-conjugated triene **36** (Scheme 6 and Table 1, entry 2). Cross-conjugated triene **36** results from a competing β -hydride elimination of rhodium metallocycle **37** to produce the alkene of intermediate **39**. The rhodium hydride of **39** then undergoes a reductive elimination to generate the exocyclic alkene of **36** as a single diastereomer. This side product has previously been observed for the formation of seven-membered rings from allenes bearing a phenylsulfonyl group.²³ Increasing the reaction temperature to 120 °C afforded dienone **35** in 61% yield and triene **36** in 35% yield (Table 1, entry 3). Decreasing the catalyst loading and increasing the reaction temperature afforded dienone **35** and triene **36** in a 1:1 ratio (Table 1, entries 4 and 5). Interestingly, the addition of silver tetrafluoroborate and triphenylphosphine afforded cyclocarbonylation product **35** in only 72% yield based upon recovered starting material. While the generality of this reaction could benefit from the lower reaction temperatures possible for the cationic Rh(I), our inability to take this reaction to completion is deemed problematic.

Transfer of Chirality in the Rh(I)-catalyzed APKR

Each of the silyl-substituted allene-ynes **13a** – **13g** was subjected to the optimized cyclocarbonylation reaction conditions. High yields of the cyclocarbonylation products were obtained for the allene-ynes bearing an internal alkyne (Table 2, entries 1 – 4, 6 and 7). The presence of heterocyclic-containing systems on the alkyne did not affect the reaction (Table 2, entries 1 and 2). Terminal alkyne **13e** was converted to cyclocarbonylation product **35e** in 66% yield, along with a 13% yield of triene **36** (Table 2, entry 5). The enantiomeric purity

of each of the allene-ynes **13a** – **13g** was based upon the enantiomeric excess obtained for allenylsilane (*R_a*)-**22**, which was determined to be greater than 93%. Each of the cycloadducts **35a** – **35g** was examined for their enantiomeric purity by HPLC analysis using a ChiralCel OD column. For each of these compounds, the enantiomeric excesses were found to be greater than 96%, constituting a complete transfer of chirality from the allene-ynes to the cyclocarbonylation products. While the transfer of chiral information may not be surprising, the high configurational stability of the dienone to the Rh(I) conditions was not anticipated.

Performing the APKR on trisubstituted allene **40** resulted in the formation the desilylated cyclocarbonylation product **41** in quantitative yield (Scheme 7).²⁴ Desilylation of α -silyl ketones have been reported to occur upon purification by silica gel chromatography.²⁵ However, it appears that desilylation of the resulting cyclocarbonylation product took place during the reaction as evidenced by crude ¹H NMR spectroscopy. Thus, the loss of the stereogenic center precluded further examination of this series of compounds.

A series a trisubstituted allenes **14**, **15** and **16** were examined in the cyclocarbonylation reaction, each possessing a phenyl group on the terminus of the allene but differing in their tether (X = NTs, O, C(CO₂Et)₂) and the substitution on the terminus of the alkyne (R = Me, Ph, TMS, cyclopropyl). The enantiomeric purity of each allene-yne was based upon the enantiomeric excess of the starting homoallenyl alcohol (*R_a*)-**29**, which was determined to be greater than 79%. For all cases examined, a complete transfer of chirality was obtained (Table 3, entries 1 – 10). For allene-ynes **14c**, **14d**, **14f** and **14g** possessing a tosylamide tether the reactions were complete in 30 minutes affording dienones **42c**, **42d**, **42f** and **42g** in 75 – 88% yield (Table 3, entries 1 – 4). The highest yielding substrate was found to be allene-yne **14g** possessing a cyclopropyl group on the terminus of the alkyne and the lowest yield was obtained with aryl-substituted substrate **14d**. For the oxygen containing tethers, the yields varied considerably (Table 3, entries 5 – 7). Methyl-substituted alkyne **15c** produced **43c** in 46% yield, phenyl-substituted alkyne **15d** afforded **43d** in 69% yield and trimethylsilyl-substituted alkyne **15f** provided **43f** in 91% yield. Furthermore, all the reactions in the oxygen-containing series were complete in less than 45 minutes. Finally, for the malonate-containing series, the yields were high for all allene-ynes and ranged from 88% to 92%. For this series (allene-ynes **16c**, **16d** and **16f**) the reactions required 120 – 150 minutes for completion, but the longer reaction time did not affect the enantioselectivity of the products. Thus, for each of the cases examined, the enantioselectivity of the products was not dependent upon the nature of the tether, the substituent on the alkyne terminus, or the reaction time.

A series of allene-ynes containing disubstituted allenes were also examined for transfer of chiral information in the cyclocarbonylation reaction. The reaction was performed using three different tethers (X = NTs, O, C(CO₂Et)₂) and varying the substitution on the terminus of the alkyne (R = Me, Ph, H, TMS). For each of the allene-ynes reported in Table 4 the enantiomeric purity was based upon the enantiomeric excess obtained for allenyl ester (*R_a*)-**27**, which was determined to be greater than 99%. Contrary to the trisubstituted allenes, the degree of chiral information transferred from the disubstituted allenes to the cyclopentenones was dependent upon the tether and alkyne substitution. For example, allene-ynes **17** – **19d** containing a phenyl group on the alkyne afforded the corresponding cyclocarbonylation products **45** – **47d** in 88% ee for the tosylamide tether (Table 4, entry 2); 52% ee for the oxygen tether (Table 4, entry 5); and 72% ee for the malonate tether (Table 4, entry 9). Furthermore, the decrease in enantiomeric excess was also dependent on the substituent on the alkyne. This was especially prevalent in the ether series of allene-ynes where the enantiomeric excesses of the cycloadducts ranged from 22 – 52% for trimethylsilyl, hydrogen, methyl or phenyl substituents (Table 4, entries 4 – 7).

Determination of the enantiomeric excesses of the cyclocarbonylation products **45** – **47** proved to be more difficult than in the trisubstituted series, in that a different chiral column was needed for nearly every product.

Insight regarding the partial racemization in the disubstituted series was obtained by reacting allene-yne **18c** to the standard conditions and allowing it to reach 60% conversion. The enantiomeric excess of the cyclocarbonylation product **46c** was measured to be 43% after purification by silica gel chromatography. The enantiomeric excess of **46c** was 45% when the reaction was allowed to go to completion, indicating that racemization of the product was not occurring after the product is formed (Table 4, entry 4). Next, the enantiomeric excess of allene-ynes **17d** and **18d** were measured during the reaction. Stopping the cyclocarbonylation reaction of **18d** at 50% conversion afforded the unreacted allene-yne in 11% ee. Similarly, stopping the reaction of allene-yne **17c** at 29% conversion afforded the allene in 15% ee. The enantiomeric excesses (ee) of the allenes were determined by HPLC analysis (ChiralPak AS-H). These three experiments provide strong evidence to support the hypothesis that loss of enantiomeric excess is occurring prior to product formation and at the allene-yne stage of the reaction.

A mechanism is proposed to account for the erosion of enantiomeric excesses of the disubstituted allenes. Inspired by the work of Backvall, addition of an internal nucleophile to a rhodium-allene complex is postulated (Scheme 8).²⁶ For the disubstituted allene **A**, coordination of the rhodium catalyst to the proximal double bond of the allene affords the rhodium complex **B**. Nucleophilic attack of the tethered heteroatom (oxygen in the example depicted) to the central carbon initially affords the corresponding η^1 -rhodium species that isomerizes to the η^3 complex **C** that in turn isomerizes to the η^1 -rhodium species **D**. Free rotation around the designated carbon-carbon bond of **D** leads to the η^3 rhodium-complex **E**. Reductive elimination from intermediate **E** leads to the formation allene-yne **F**, the enantiomer of allene-yne **A**. Erosion in the enantiomeric excesses correlates well with the relative nucleophilicities of the heteroatoms in the tether. For example, the highest enantiomeric excesses were obtained for the cyclocarbonylation products with a tosylamide tether whereas the lowest enantiomeric excesses were obtained for the oxygen tether. In the case of the malonate tether, formation of an intermediate seven-membered ring would explain the racemization process.

For the trisubstituted allene series, the absence of racemization is explained by selective complexation of the rhodium catalyst with the less substituted distal double bond of the allene and complexation from the face opposite of the DPS group (intermediate **G**, Scheme 8). Moreover, the rhodium metallocycle of intermediate **G** is not set up for an internal nucleophilic addition but instead is well positioned to undergo complexation with alkyne, ultimately affording the desired cyclocarbonylation product with no loss in enantiomeric excesses.

Determination of the Absolute Configuration of the Cyclocarbonylation Product

The fortuitous crystallization of **35c** at $-20\text{ }^{\circ}\text{C}$ allowed for the determination of the absolute configuration by X-ray diffraction using the anomalous scattering effect of the silicon and is in agreement with the absolute configuration of that established for allenyl alcohol (R_a)-**22** (Scheme 9).²⁷

Furthermore, during attempts to establish the absolute configuration of cyclocarbonylation product **35e** by derivatization with (*S*)-(-)-1-amino-2-(methoxymethyl)pyrrolidine (SAMP), compound **48** was isolated instead of the expected hydrazone (Scheme 10). Structurally similar compounds are usually synthesized by performing the APKR on allenamides.²⁸ This type of isomerization has previously been observed during an APKR.²⁸ The silicon group is

shown to have no effect on this unusual isomerization since compound **48** was also obtained when the reaction was performed on the dienone lacking the silicon group.

Conclusion

In summary, we have successfully performed a transfer of chirality from a chiral non-racemic allene to a 4-alkylidene cyclopentenone in a Rh(I)-catalyzed APKR. Complete transfer of chirality was obtained for every trisubstituted allene. Investigations regarding the loss of enantiomeric excess observed when the APKR was performed with disubstituted allene-yne demonstrated that partial racemization of the allenes was occurring during the reaction. Moreover, the mildness of the reaction conditions are highlighted by the absence of epimerization of the stereogenic center during the reaction. The absolute configuration of cyclocarbonylation product **35c** was unambiguously established by X-ray crystallographic analysis. The absolute configuration of this dienone corresponds to the predicted assignment, based upon the absolute configuration of the propargylic alcohol precursor. Finally, an unusual isomerization of the dienone was observed during attempts to functionalize the carbonyl group, affording a presumably more stable vinylogous amide.

Experimental Section

Unless otherwise noted, all reactions were performed under N₂ in flame-dried glassware using standard syringe, cannula, and septum techniques. All commercially available compounds were used as received unless otherwise noted. The reaction solvents tetrahydrofuran (THF) and dichloromethane (CH₂Cl₂) were obtained by passing commercially available predried, oxygen-free formulations through activated alumina columns. Toluene, acetonitrile, 2,6-lutidine and triethylamine (Et₃N) were freshly distilled from CaH₂ prior to use. *N,N*-dimethylacetamide was dried over 4 Å molecular sieves for 12 h prior to use. Flash chromatography was carried out on silica. Thin layer chromatography (TLC) analysis was performed on precoated silica gel F₂₅₄ aluminium plates. ¹H NMR and ¹³C NMR spectra were recorded in deuterated solvents and referenced to residual chloroform (7.26 ppm, ¹H, 77.0 ppm, ¹³C). Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Coupling constants, *J*, are reported in hertz. All NMR spectra were obtained at rt. Infrared spectra were recorded neat and are reported in cm⁻¹. HRMS data were collected using a TOF mass spectrometer.

General Procedure for Preparation of Allene-yne *via* Mitsunobu Reaction

To a solution of the alcohol in THF cooled to 0 °C (ice bath) was added triphenylphosphine (1.2 equiv), the tosylamide (1.2 equiv) and diisopropylazodicarboxylate (1.2 equiv). The reaction mixture was stirred until completion as judged by TLC analysis. Concentration of the reaction mixture under reduced pressure afforded the crude residue. The crude material was purified by flash chromatography.

General Procedure for Preparation of Allene-yne *via* Williamson Etherification

A solution of the alcohol in THF was cooled to 0 °C (ice bath) and sodium hydride (2 equiv, 60% dispersion in mineral oil) was added portionwise. The mixture was stirred for 30 min at rt. The propargyl bromide (1.5 equiv) was added and the reaction was stirred at rt until completion as judged by TLC analysis. The reaction was quenched by careful dropwise addition of water over 5 min. The two layers were separated and the aqueous layer was extracted with Et₂O. The organic layers were combined, dried (Na₂SO₄), filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography.

General Procedure for Preparation of Allene-yne *via* Alkylation of the Malonate Moiety

The diethyl malonate²³ (2 equiv) was added dropwise to a stirred suspension of sodium hydride (2 equiv, 60% dispersion in mineral oil) in a DMF/THF (1:1) mixture cooled to 0 °C (ice bath). After 1 h at 0 °C, hydrogen evolution had ceased and the mesylate (1 equiv) in THF was added, followed by potassium iodide (1.5 equiv). The reaction mixture was stirred at 70 °C for 12 h. The solution was cooled to rt, diluted with Et₂O and quenched by careful dropwise addition of a saturated solution of NH₄Cl. The layers were separated and the aqueous layer was extracted with Et₂O. The combined organic phases were washed with brine, dried (Na₂SO₄), filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography.

General Procedure for Preparation of Allene-yne *via* Silylation of the Terminal Alkyne

To a solution of the allene-yne (1 equiv) in THF cooled to –78 °C was added lithium hexamethyldisilylamide (1 M in THF, 1.3 equiv) and the resulting mixture was stirred at –78 °C for 1 h. Trimethylsilyl chloride (2 equiv) was then added and the reaction was stirred for 1 h at –78 °C. The mixture was quenched with a saturated solution of NH₄Cl and diluted with Et₂O. The layers were separated and the aqueous layer was extracted with Et₂O. The combined organic phases were washed with brine, dried (Na₂SO₄), filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography.

General Procedure for the [Rh(CO)₂Cl]₂-Catalyzed Cyclocarbonylation Reaction

A flame dried vial (15 × 45 mm) equipped with a Teflon-coated stir-bar and a septa cap was charged with allene-yne and toluene (0.1 M). The tube was evacuated for 3–5 sec. and refilled with CO (g) (3 ×) using a balloon. To the allene-yne solution was added [Rh(CO)₂Cl]₂ (0.1 equiv) in one portion, and the vial was evacuated and refilled with CO (g) (3 ×). The vial was placed in a preheated 90 °C oil bath and stirred under CO (g). After the reaction was complete as judged by TLC analysis, the mixture was cooled to rt, passed through a short plug of Celite using Et₂O, and concentrated under reduced pressure. The crude material was purified by flash chromatography.

(*R_a*)-Hexa-3,4-dien-1-yl 4-nitrobenzoate (**27**)

(*R_a*)-hexa-3,4-dien-1-ol³² **26** (48 mg, 0.49 mmol) was dissolved in *N,N*-dimethylacetamide (0.9 mL) and 2,6-lutidine (150 μL, 1.32 mmol). This solution was added dropwise to a solution of *p*-nitrobenzoyl chloride (118 mg, 0.64 mmol), 4-*N,N*-dimethylaminopyridine (12 mg, 0.098 mmol) in acetonitrile (0.7 mL) at 0 °C (ice bath). After completion of the addition, the reaction mixture was stirred for 1 h at 0 °C. After quenching with a saturated solution of sodium bicarbonate (3 mL), the mixture was extracted with Et₂O (20 mL), washed with water (5 mL), brine (5 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, gradient of 1–10% Et₂O/hexanes) afforded compound **27** (73.4 mg, 61%) as a colorless oil. ¹H NMR (700 MHz, CDCl₃) δ 8.29 (d, *J* = 8.7 Hz, 2H), 8.22 (d, *J* = 8.7 Hz, 2H), 5.12 – 5.10 (m, 2H), 4.45 – 4.43 (m, 2H), 2.48 – 2.43 (m, 2H), 1.62 – 1.61 (m, 3H); ¹³C NMR (175 MHz, CDCl₃) δ 205.5, 164.6, 150.5, 135.7, 130.6 (2C), 123.5 (2C), 86.6, 85.8, 64.9, 28.2, 14.3; IR (thin film) 3113, 2954, 2901, 2852, 1965, 1720, 1532, 1352, 1274, 1103, 1111, 1013, 874; HRMS (ES+) C₂H₁₃NO₄ [M⁺]

Calculated: 247.0845; Found: 247.0867; [α]_D²⁰ = –43.6° (c 0.55, CH₂Cl₂).

(*R_a*)-*N*-(hexa-3,4-dien-1-yl)-4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzene sulfonamide (**17d**)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, (*R_a*)-hexa-3,4-dien-1-ol **26** (26.4 mg, 0.27 mmol) in THF (1.9 mL) was reacted with

triphenylphosphine (85 mg, 0.32 mmol), 4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide³² (92.1 mg, 0.32 mmol) and diisopropylazodicarboxylate (64 μ L, 0.32 mmol) for 12 h. Purification of the crude residue using a Biotage normal phase automated purification system (25 g SNAP column, gradient of 0 – 20% Et₂O/hexanes) afforded compound **17d** (83.9 mg, 85%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.28 – 7.22 (m, 5H), 7.08 (d, *J* = 7.3 Hz, 2H), 5.11 – 5.08 (m, 1H), 5.08 – 5.03 (m, 1H), 4.36 (s, 2H), 3.33 (t, *J* = 7.3 Hz, 2H), 2.34 (s, 3H), 2.32 – 2.31 (m, 2H), 1.66 – 1.64 (m, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 205.4, 143.3, 136.0, 131.5 (2C), 129.5 (2C), 128.4, 128.1 (2C), 127.7 (2C), 122.2, 86.6, 86.4, 85.6, 81.9, 46.1, 37.3, 27.6, 21.4, 14.4; IR (thin film) 3060, 3031, 2987, 2921, 2856, 2235, 1973, 1597, 1487, 1438, 1344, 1168, 1095, 1025, 907; HRMS (ES+) C₂₂H₂₃NO₂NaS [M+Na] Calculated: 388.1347; Found: 388.1364; [α]_D²⁰ = – 25.5° (c 1.45, CH₂Cl₂).

(S)-6-methyl-8-phenyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[*c*]azepin-7(6*H*)-one (45d)

Following the general procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **17d** (40.4 mg, 0.11 mmol) and [Rh(CO)₂Cl]₂ (4.3 mg, 0.011 mmol) were reacted in toluene (3.4 mL) for 180 min. Purification of the crude residue using a Biotage normal phase automated purification system (10 g SNAP column, 70% Et₂O/hexanes) afforded compound **45d** (36.5 mg, 84%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 7.54 – 7.53 (m, 2H), 7.46 – 7.45 (m, 2H), 7.41 – 7.39 (m, 1H), 7.29 (d, *J* = 6.9 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.79 – 5.77 (m, 1H), 4.60 – 4.53 (m, 2H), 3.67 – 3.63 (m, 1H), 3.63 – 3.61 (m, 1H), 2.78 – 2.77 (m, 1H), 2.70 – 2.68 (m, 2H), 2.40 (s, 3H), 1.17 (d, *J* = 7.5 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 205.3, 160.2, 143.5, 141.2, 140.7, 136.5, 130.4, 129.6 (2C), 129.3 (2C), 128.7, 128.5 (2C), 127.0 (2C), 125.5, 49.1, 49.0, 45.2, 30.8, 21.5, 15.0; IR (thin film) 3060, 2974, 2925, 2876, 1699, 1601, 1499, 1450, 1336, 1160, 1095, 952; HRMS (ES+) C₂₃H₂₄NO₃S [M+H⁺] Calculated: 394.1477; Found: 394.1473; [α]_D²⁰ = +1.64° (c 1.4, CH₂Cl₂).

(*R_a*)-*N*-(hexa-3,4-dien-1-yl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (17e)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, (*R_a*)-hexa-3,4-dien-1-ol **26** (42.1 mg, 0.43 mmol) in THF (3 mL) was reacted with triphenylphosphine (135 mg, 0.51 mmol), 4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide³² (108 mg, 0.51 mmol) and diisopropylazodicarboxylate (101 μ L, 0.51 mmol) for 6 h. Purification of the crude residue using a Biotage normal phase automated purification system (12 g SNAP column, gradient of 5 – 10% Et₂O/hexanes) afforded compound **17e** (105 mg, 84%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 5.10 – 5.07 (m, 1H), 5.02 – 4.99 (m, 1H), 4.14 (d, *J* = 2.5 Hz, 2H), 3.26 (t, *J* = 7.4 Hz, 2H), 2.42 (s, 3H), 2.26 (m, 2H), 2.03 (t, *J* = 2.5 Hz, 1H), 1.65 – 1.63 (m, 3H); ¹³C NMR (175 MHz, CD₂Cl₂) δ 205.2, 143.7, 136.0, 129.5 (2C), 127.6 (2C), 86.5, 86.3, 76.7, 73.4, 46.1, 36.4, 27.5, 21.3, 14.2; IR (thin film) 3289, 2974, 2925, 2856, 1960, 1593, 1454, 1344, 1160, 1102; HRMS (ES+) C₁₆H₂₀NO₂S [M+H⁺] Calculated: 290.1215; Found: 290.1237; [α]_D²⁰ = – 37.6° (c 1.25, CH₂Cl₂).

(*R_a*)-*N*-(hexa-3,4-dien-1-yl)-4-methyl-*N*-(3-(trimethylsilyl)prop-2-yn-1-yl)benzene sulfonamide (17f)

Following the general procedure for preparation of allene-yne *via* silylation of the terminal alkyne, allene-yne **17e** (70 mg, 0.24 mmol) in THF (1.8 mL) was reacted with lithium hexamethyldisilylamide (314 μ L, 1M in THF, 0.31 mmol) and trimethylsilylchloride (61 μ L, 0.48 mmol). Purification of the crude residue using a Biotage normal phase automated purification system (10 g SNAP column, gradient of 2 – 7% Et₂O/hexanes) afforded

compound **17f** (73.2 mg, 84%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.72 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 7.9 Hz, 2H), 5.09 – 5.02 (m, 2H), 4.15 (s, 2H), 3.25 (t, J = 7.4 Hz, 2H), 2.42 (s, 3H), 2.28 – 2.25 (m, 2H), 1.66 – 1.63 (m, 3H), –0.01 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 205.3, 143.2, 135.9, 129.4 (2C), 127.7 (2C), 97.9, 90.8, 86.5, 86.3, 45.8, 37.3, 27.4, 21.5, 14.4, –0.5 (3C); IR (thin film) 2965, 2916, 2857, 2178, 1594, 1455, 1249, 1346, 115536, 1095; HRMS (ES+) $\text{C}_{19}\text{H}_{28}\text{NO}_2\text{SSi}$ $[\text{M}+\text{H}^+]$ Calculated: 362.1610; Found: 362.1628; $[\alpha]_{\text{D}}^{20}$ = – 27.6° (c 1.05, CH_2Cl_2).

(S)-6-methyl-2-tosyl-8-(trimethylsilyl)-1,2,3,4-tetrahydrocyclopenta[c]azepin-7(6H)-one (45f)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **17f** (42 mg, 0.12 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (4.5 mg, 0.012 mmol) were reacted in toluene (3.6 mL) for 180 min. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, 65% Et_2O /hexanes) afforded compound **45f** (37.5 mg, 83%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.64 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.3 Hz, 2H), 5.70 – 5.67 (m, 1H), 4.53 (s, 2H), 3.56 – 3.52 (m, 2H), 2.64 – 2.59 (m, 3H), 2.41 (s, 3H), 1.07 (d, J = 7.5 Hz, 3H), 0.30 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 211.3, 172.6, 143.6, 143.5, 141.9, 136.2, 129.7 (2C), 127.1 (2C), 124.8, 50.6, 48.8, 46.1, 31.0, 21.5, 14.9, –0.5 (3C); IR (thin film) 2958, 2921, 2864, 1691, 1536, 1340, 1164, 1091; HRMS (ES+) $\text{C}_{20}\text{H}_{28}\text{NO}_3\text{SSi}$ $[\text{M}+\text{H}^+]$ Calculated: 390.1559; Found: 390.1549; $[\alpha]_{\text{D}}^{20}$ = +8.3° (c 0.8, CH_2Cl_2).

(R_a)-N-(but-2-yn-1-yl)-N-(hexa-3,4-dien-1-yl)-4-methylbenzenesulfonamide (17c)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, (*R_a*)-hexa-3,4-dien-1-ol **26** (25 mg, 0.26 mmol) in THF (1.8 mL) was reacted with triphenylphosphine (80.2 mg, 0.31 mmol), *N*-(but-2-yn-1-yl)-4-methylbenzenesulfonamide³² (68.3 mg, 0.31 mmol) and diisopropylazodicarboxylate (61 μL , 0.31 mmol) for 12 h. Purification of the crude residue using a Biotage normal phase automated purification system (10 g SNAP column, gradient of 10% Et_2O /hexanes) afforded compound **17c** (57 mg, 74%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.73 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 5.08 – 5.04 (m, 1H), 5.04 – 4.99 (m, 1H), 4.07 – 4.06 (m, 2H), 3.26 – 3.21 (t, J = 7.3 Hz, 2H), 2.42 (s, 3H), 2.26 – 2.23 (m, 2H), 1.66 – 1.63 (m, 3H), 1.57 – 1.55 (t, J = 2.4 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 205.3, 143.1, 136.1, 129.2 (2C), 127.8 (2C), 86.6, 86.3, 81.4, 71.8, 45.9, 36.9, 27.6, 21.5, 14.4, 3.2; IR (thin film) 2925, 2852, 1961, 1597, 1442, 1348, 1160, 1099; HRMS (ES+) $\text{C}_{17}\text{H}_{22}\text{NO}_2\text{S}$ $[\text{M}+\text{H}^+]$ Calculated: 304.1371; Found: 304.1363; $[\alpha]_{\text{D}}^{20}$ = – 17.7° (c 2.6, CH_2Cl_2).

(S)-6,8-Dimethyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[c]azepin-7(6H)-one (45c)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **17c** (16.9 mg, 0.056 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (2.2 mg, 0.0056 mmol) were reacted in toluene (1.7 mL) for 280 min. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, 70% Et_2O /hexanes) afforded compound **45c** (13.5 mg, 73%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.66 (d, J = 8.3 Hz, 2H), 7.29 – 7.26 (d, J = 8.3 Hz, 2H), 5.63 (t, J = 5.0 Hz, 1H), 4.43 – 4.41 (m, 2H), 3.55 – 3.51 (m, 2H), 2.70 – 2.59 (m, 3H), 2.42 (s, 3H), 1.81 (s, 3H), 1.10 (d, J = 7.4 Hz, 3H); ^{13}C NMR (175 MHz, CDCl_3) 207.0, 159.8, 143.6, 140.8, 138.0, 136.2, 129.7 (2C), 127.0 (2C), 123.7, 49.0, 48.9, 44.6, 31.3, 21.5, 14.9, 8.4; IR (thin film) 2062, 2921, 2856, 2002, 1691, 1597, 1446, 1340, 1164, 1095; HRMS (ES+) $\text{C}_{18}\text{H}_{22}\text{NO}_3\text{S}$ $[\text{M}+\text{H}^+]$ Calculated: 332.1320; Found: 332.1347; $[\alpha]_{\text{D}}^{20}$ = +2.4° (c 0.85, CH_2Cl_2).

(*R_a*)-Hexa-3,4-dien-1-yl methanesulfonate (32)

To a stirred solution of (*R_a*)-hexa-3,4-dien-1-ol **26** (60.8 mg, 0.62 mmol) in THF (8.7 mL), cooled to 0 °C (ice bath), was added triethylamine (95 μ L, 0.68 mmol) followed by methanesulfonyl chloride (53 μ L, 0.681 mmol). The resulting solution was stirred at rt for 12 h. The mixture was diluted with Et₂O (60 mL), washed with water (2 $\times$ 10 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure. Purification of the crude residue using a Biotage normal phase automated purification system (12 g SNAP column, 35% Et₂O/hexanes) afforded compound **32** (84.1 mg, 77%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.22 – 5.12 (m, 1H), 5.05 – 5.03 (m, 1H), 4.25 (t, *J* = 6.8 Hz, 2H), 3.00 (s, 3H), 2.44 – 2.39 (m, 2H), 1.65 (dd, *J* = 7.0, 3.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 205.4, 86.9, 84.8, 69.0, 37.2, 28.5, 14.1; IR (thin film) 3032, 2987, 2942, 1965, 1462, 1344, 1172, 964, 911; HRMS (ES+) C₇H₁₃O₃S [M+H⁺] Calculated: 177.0585; Found: 177.0588; [α]_D²⁰ = – 32.4° (c 1.45, CH₂Cl₂).

(*R_a*)-Diethyl 2-(hexa-3,4-dien-1-yl)-2-(3-phenylprop-2-yn-1-yl)malonate (19d)

Following the General Procedure for Preparation of Allene-yne *via* alkylation of the malonate moiety, diethyl malonate **34d** (79.3 mg, 0.29 mmol) was reacted with sodium hydride (8.7 mg, 60 wt% in oil, 0.22 mmol), mesylate **32** (25.5 mg, 0.15 mmol) and potassium iodide (36 mg, 0.22 mmol) in DMF-THF (1 : 1, 4 mL). Purification of the crude residue using a Biotage normal phase automated purification system (25 g SNAP column, gradient of 3 – 7% Et₂O/hexanes) afforded compound **19d** (35.4 mg, 69%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.38 – 7.35 (m, 2H), 7.29 – 7.27 (m, 3H), 5.09 – 5.05 (m, 2H), 4.22 (q, *J* = 7.2 Hz, 4H), 3.05 (s, 2H), 2.25 – 2.20 (m, 2H), 1.98 – 1.95 (m, 2H), 1.65 – 1.62 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 6H); ¹³C NMR (175 MHz, CDCl₃) δ 204.6, 170.3 (2C), 131.6 (2C), 128.1 (2C), 127.9, 123.3, 89.4, 86.4, 84.4, 83.4, 61.5 (2C), 56.9, 31.6, 23.8, 23.7, 14.4, 14.1 (2C); IR (thin film) 3465, 2987, 2921, 2856, 1965, 1732, 1597, 1487, 1446, 1368, 1270, 1197, 1091, 1030; HRMS (ES+) C₂₂H₂₇O₄ [M+H⁺] Calculated: 355.1909; Found: 355.1885; [α]_D²⁰ = – 19.6° (c 2.5, CH₂Cl₂).

(*S*)-Diethyl 1-methyl-2-oxo-3-phenyl-1,2,6,7-tetrahydroazulene-5,5(4*H*)-dicarboxylate (47d)

Following the General Procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **19d** (22.6 mg, 0.064 mmol) and [Rh(CO)₂Cl]₂ (2.5 mg, 0.0064 mmol) were reacted in toluene (2 mL) for 100 min. Purification of the residue by flash chromatography (45% Et₂O/hexanes) afforded the title compound **47d** (23.3 mg, 96%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.44 – 7.26 (m, 5H), 6.04 – 5.92 (m, 1H), 4.15 – 4.02 (m, 4H), 3.39 (s, 2H), 2.94 – 2.87 (q, *J* = 7.4 Hz, 1H), 2.56 – 2.52 (m, 2H), 2.45 – 2.41 (m, 2H), 1.27 (d, *J* = 7.5 Hz, 3H), 1.13 (q, *J* = 7.1 Hz, 6H); ¹³C NMR (175 MHz, CDCl₃) δ 206.0, 171.1, 170.9, 161.3, 143.2, 141.9, 131.3, 129.4 (2C), 128.3 (2C), 128.2, 127.9, 61.7, 61.6, 56.3, 44.9, 34.5, 33.8, 25.1, 15.3, 13.9, 13.8; IR (thin film) 2966, 2929, 2852, 2365, 1732, 1699, 1450, 1364, 1242, 1176, 1078; HRMS (ES+) C₂₃H₂₇O₅ [M+H⁺] Calculated: 383.1858; Found: 383.1860; [α]_D²⁰ = – 12.6° (c 0.95, CH₂Cl₂).

(*R_a*)-Diethyl 2-(but-2-yn-1-yl)-2-(hexa-3,4-dien-1-yl)malonate (19c)

Following the General Procedure for Preparation of Allene-yne *via* alkylation of the malonate moiety, diethyl malonate **34c** (94.4 mg, 0.45 mmol) was reacted with sodium hydride (15.3 mg, 60 wt% in oil, 0.38 mmol), mesylate **32** (56 mg, 0.32 mmol) and potassium iodide (79.1 mg, 0.48 mmol) in DMF-THF (1 : 1, 6 mL). Purification of the crude residue using a Biotage normal phase automated purification system (25 g SNAP column, gradient of 4 – 6% Et₂O/hexanes) afforded compound **19c** (59.6 mg, 63%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.07 – 5.02 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 4H), 2.75 (s,

2H), 2.12 – 2.10 (m, 2H), 1.90 – 1.88 (m, 2H), 1.73 (s, 3H), 1.64 – 1.62 (m, 3H), 1.23 (t, J = 7.2 Hz, 6H); ^{13}C NMR (175 MHz, CDCl_3) δ 204.6, 170.4 (2C), 89.4, 86.3, 78.5, 73.4, 61.3 (2C), 56.8, 31.4, 23.7, 23.1, 14.4, 14.0 (2C), 3.4; IR (thin film) 2983, 2934, 2859, 1736, 1438, 1360, 1275, 1225, 1193; HRMS (ES+) $\text{C}_{17}\text{H}_{25}\text{O}_4$ $[\text{M}+\text{H}^+]$ Calculated: 293.1753; Found: 293.1778; $[\alpha]_{\text{D}}^{20}$ = -32.9° (c 0.85, CH_2Cl_2).

(S)-diethyl 1,3-dimethyl-2-oxo-1,2,6,7-tetrahydroazulene-5,5(4H)-dicarboxylate (47c)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **19c** (33.8 mg, 0.11 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (4.4 mg, 0.011 mmol) were reacted in toluene (3.6 mL) for 22 h. Purification of the residue by flash chromatography (40% Et_2O /hexanes) afforded compound **47c** (25.7 mg, 71%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 5.81 – 5.79 (m, 1H), 4.23 – 4.15 (m, 4H), 3.21 (s, 2H), 2.76 – 2.68 (m, 1H), 2.51 – 2.47 (m, 2H), 2.39 – 2.33 (m, 2H), 1.84 (s, 3H), 1.27 – 1.22 (m, 6H), 1.16 (d, J = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 208.1, 171.3, 171.2, 161.0, 143.6, 139.2, 125.9, 61.7 (2C), 56.2, 44.2, 33.9 (2C), 25.0, 15.0, 14.0 (2C), 8.3; IR (thin film) 2978, 2921, 1732, 1703, 1446, 1364, 1287, 1234, 1062, 1095; HRMS (ES+) $\text{C}_{18}\text{H}_{25}\text{O}_5$ $[\text{M}+\text{H}^+]$ Calculated: 321.1702; Found: 321.1723; $[\alpha]_{\text{D}}^{20}$ = -12° (c 0.5, CH_2Cl_2).

(R_a)-Diethyl 2-(hexa-3,4-dien-1-yl)-2-(prop-2-yn-1-yl)malonate (19e)

Following the General Procedure for Preparation of Allene-yne *via* alkylation of the malonate moiety, diethyl malonate **34e** (189 mg, 0.95 mmol) was reacted with sodium hydride (28.6 mg, 60 wt% in oil, 0.71 mmol), mesylate **32** (84 mg, 0.48 mmol) and potassium iodide (119 mg, 0.72 mmol) in DMF-THF (1 : 1, 13 mL). Purification of the crude residue using a Biotage normal phase automated purification system (50 g SNAP column, gradient of 2 – 7% Et_2O /hexanes) afforded compound **19e** (75.5 mg, 57%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 5.09 – 5.03 (m, 2H), 4.24 – 4.17 (m, 4H), 2.83 (s, 2H), 2.20 – 2.14 (m, 2H), 2.00 (t, J = 2.7 Hz, 1H), 1.96 – 1.87 (m, 2H), 1.66 – 1.63 (m, 3H), 1.25 (t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 204.5, 170.0 (2C), 89.3, 86.3, 78.9, 71.0, 61.6 (2C), 56.4, 31.3, 23.7, 22.7, 14.2, 13.8 (2C); IR (thin film) 3293, 2892, 2938, 1736, 1454, 1270, 1193, 1095, 1030. HRMS (ES+) $\text{C}_{16}\text{H}_{23}\text{O}_4$ $[\text{M}+\text{H}^+]$ Calculated: 279.1596; Found: 279.1623; $[\alpha]_{\text{D}}^{20}$ = -40° (c 2.2, CH_2Cl_2).

(R_a)-Diethyl 2-(hexa-3,4-dien-1-yl)-2-(3-(trimethylsilyl)prop-2-yn-1-yl)malonate (19f)

Following the general procedure for preparation of allene-yne *via* silylation of the terminal alkyne, allene-yne **19e** (67.6 mg, 0.24 mmol) in THF (1.8 mL) was reacted with lithium hexamethyldisilylamide (365 μL , 1M in THF, 0.36 mmol) and trimethylsilylchloride (62 μL , 0.49 mmol). Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, 5% Et_2O /hexanes) afforded compound **19f** (74.4 mg, 88%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 5.08 – 5.03 (m, 2H), 4.20 – 4.17 (m, 4H), 2.84 (s, 2H), 2.14 – 2.12 (m, 2H), 1.93 – 1.90 (m, 2H), 1.65 – 1.62 (m, 3H), 1.24 (t, J = 7.1 Hz, 6H), 0.12 (s, 9H); ^{13}C NMR (175 MHz, CDCl_3) δ 204.6, 170.1 (2C), 101.4, 89.4, 88.0, 86.3, 61.5 (2C), 56.7, 31.4, 24.2, 23.7, 14.4, 14.0 (2C), -0.1 (3C); IR (thin film) 2958, 2925, 2860, 2186, 1740, 1471, 1442, 1254, 1197, 1103, 1034, 854; HRMS (ES+) $\text{C}_{19}\text{H}_{31}\text{O}_4\text{Si}$ $[\text{M}+\text{H}^+]$ Calculated: 351.1992; Found: 351.1990; $[\alpha]_{\text{D}}^{20}$ = -30.3° (c 1.85, CH_2Cl_2).

(S)-Diethyl 1-methyl-2-oxo-3-(trimethylsilyl)-1,2,6,7-tetrahydroazulene-5,5(4H)-dicarboxylate (47f)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **19f** (33.9 mg, 0.097 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (2.5 mg, 0.0097 mmol)

were reacted in toluene (3.2 mL) for 10 h. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, 25% Et₂O/hexanes) afforded compound **47f** (34.5 mg, 94%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 5.88 – 5.83 (m, 1H), 4.23 – 4.16 (m, 4H), 3.37 – 3.36 (m, 2H), 2.75 – 2.68 (m, 1H), 2.50 – 2.46 (m, 2H), 2.40 – 2.34 (m, 2H), 1.24 (td, *J* = 7.1, 0.9 Hz, 6H), 1.14 (t, *J* = 7.4 Hz, 3H), 0.27 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 212.3, 173.4, 171.1, 171.0, 145.6, 142.8, 127.3, 61.7, 61.6, 56.3, 46.1, 36.5, 33.7, 25.2, 15.0, 14.0 (2C), –0.3 (3C); IR (Thin film) 2970, 2929, 2905, 1736, 1691, 1540, 1446, 1368, 1291, 1230, 1078, 1037, 841; HRMS (ES+) C₂₀H₃₁O₅Si [M+H⁺] Calculated: 379.1941; Found: 379.1967; [α]_D²⁰ = – 5.5° (c 2.2, CH₂Cl₂).

(R_a)-6-(But-2-yn-1-yloxy)hexa-2,3-diene (18c)

Following the general procedure for preparation of allene-yne *via* Williamson etherification, (*R_a*)-hexa-3,4-dien-1-ol **26** (32.3 mg, 0.33 mmol) in THF (0.8 mL) was reacted with sodium hydride (26.5 mg, 60% dispersion in mineral oil 0.66 mmol) and 1-bromobut-2-yne (61.3 mg, 0.46 mmol) for 12 h. Purification of the crude residue using a Biotage normal phase automated purification system (12 g SNAP column, gradient of 0 – 3% Et₂O/hexanes) afforded compound **18c** (37.4 mg, 83%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 5.09 – 5.04 (m, 2H), 4.10 – 4.08 (m, 2H), 3.56 – 3.51 (m, 2H), 2.29 – 2.25 (m, 2H), 1.86 – 1.84 (m, 3H), 1.66 – 1.62 (m, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 205.2, 86.6, 85.8, 82.1, 75.2, 69.3, 58.5, 29.1, 14.3, 3.5; IR (thin film) 2925, 2860, 1446, 1356, 1140, 1095; HRMS (ES+) C₁₀H₁₅O [M+H⁺] Calculated: 151.1123; Found: 151.1150; [α]_D²⁰ = – 20.5° (c 1.85, CH₂Cl₂).

(S)-6,8-Dimethyl-3,4-dihydro-1H-cyclopenta[c]oxepin-7(6H)-one (46c)

Following the General Procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **18c** (27.1 mg, 0.20 mmol) and [Rh(CO)₂Cl]₂ (7.6 mg, 0.020 mmol) were reacted in toluene (6.4 mL) for 390 min. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, 60% Et₂O/hexanes) afforded compound **46c** (14.1 mg, 40%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 5.79 – 5.76 (m, 1H), 4.74 (s, 2H), 3.94 (t, *J* = 5.3 Hz, 2H), 2.87 – 2.74 (m, 1H), 2.63 – 2.58 (m, 2H), 1.74 (s, 3H), 1.23 (d, *J* = 7.5 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 207.2, 164.0, 140.6, 136.2, 124.6, 71.6, 71.0, 44.6, 33.8, 15.2, 8.1; IR (thin film) 2966, 2925, 2872, 1695, 1597, 1458, 1372, 1328, 1225, 1205, 1140; HRMS (ES+) C₁₁H₁₅O₂ [M+H⁺] Calculated: 179.1072; Found: 179.1051; [α]_D²⁰ = +2.9° (c 1.05, CH₂Cl₂).

(R_a)-6-(Prop-2-yn-1-yloxy)hexa-2,3-diene (18e)

Following the general procedure for preparation of allene-yne *via* Williamson etherification (*R_a*)-hexa-3,4-dien-1-ol **26** (70.7 mg, 0.72 mmol) in THF (1.7 mL) was reacted with sodium hydride (58 mg, 60% dispersion in mineral oil 1.44 mmol) and propargyl bromide (161 mg, 80 wt% in toluene, 1.08 mmol) for 11 h. Purification of the crude residue using a Biotage normal phase automated purification system (12 g SNAP column, gradient of 0 – 2% Et₂O/hexanes) afforded compound **18e** (43.4 mg, 44%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 5.09 – 5.06 (m, 2H), 4.16 (d, *J* = 2.4 Hz, 2H), 3.58 (t, *J* = 6.8 Hz, 2H), 2.42 (t, *J* = 2.4 Hz, 1H), 2.30 – 2.26 (m, 2H), 1.66 – 1.64 (m, 3H); ¹³C NMR (150 MHz, CD₂Cl₂) δ 205.1, 86.6, 85.8, 80.0, 73.8, 69.4, 57.9, 29.2, 14.2; IR (thin film) 2933, 2852, 1454, 1356, 1099; HRMS (ES+) C₉H₁₁O [M–H⁺] Calculated: 135.0810; Found: 135.0835; [α]_D²⁰ = – 41.5° (c 1.35, CH₂Cl₂).

(S)-6-Methyl-3,4-dihydro-1H-cyclopenta[c]oxepin-7(6H)-one (46e)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **18e** (45.5 mg, 0.33 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (13 mg, 0.033 mmol) were reacted in toluene (10.9 mL) for 105 min. Purification of the crude residue using a Biotage normal phase automated purification system (10 g SNAP column, 20 – 65% Et_2O /hexanes) afforded compound **46e** (13.3 mg, 24%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 6.00 (s, 1H), 5.91 – 5.89 (m, 2H), 4.78 – 4.77 (m, 2H), 3.96 – 3.92 (m, 2H), 2.88 – 2.84 (m, 1H), 2.63 – 2.61 (m, 1H), 1.25 (d, $J = 7.6$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 207.6, 171.4, 141.6, 127.9, 127.6, 71.9, 71.8, 45.8, 33.8, 15.0; IR (thin film) 2925, 2864, 1699, 1565, 1458, 1368, 1201, 1120, 1070; HRMS (ES+) $\text{C}_{10}\text{H}_{13}\text{O}_2$ $[\text{M}+\text{H}^+]$ Calculated: 165.0916; Found: 165.0897; $[\alpha]_{\text{D}}^{20} = +14.1^\circ$ (c 0.85, CH_2Cl_2).

(R_a)-(3-(Hexa-3,4-dien-1-yloxy)prop-1-yn-1-yl)trimethylsilane (18f)

Following the general procedure for preparation of allene-yne *via* silylation of the terminal alkyne, allene-yne **18e** (72.4 mg, 0.53 mmol) in THF (4.2 mL) was reacted with lithium hexamethyldisilylamide (798 μL , 1M in THF, 0.80 mmol) and trimethylsilyl chloride (135 μL , 1.06 mmol). Purification of the crude residue using a Biotage normal phase automated purification system (10 g SNAP column, gradient of 0 – 1% Et_2O /hexanes) afforded compound **18f** (76 mg, 69%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 5.10 – 5.05 (m, 2H), 4.15 (s, 2H), 3.56 (t, $J = 6.8$ Hz, 2H), 2.30 – 2.26 (m, 2H), 1.64 – 1.63 (m, 3H), 0.18 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 205.3, 101.7, 91.1, 86.7, 85.9, 69.5, 58.8, 29.1, 14.4, –0.2 (3C); IR (thin film) 2954, 2897, 2178, 1258, 1107, 919, 850; HRMS (ES+) $\text{C}_{12}\text{H}_{20}\text{OSi}$ $[\text{M}-\text{H}]^+$ Calculated: 207.1205; Found: 207.1189; $[\alpha]_{\text{D}}^{20} = -33.3^\circ$ (C 1.35, CH_2Cl_2).

(S)-6-Methyl-8-(trimethylsilyl)-3,4-dihydro-1H-cyclopenta[c]oxepin-7(6H)-one (46f)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed cyclocarbonylation Reaction, allene-yne **18f** (29.8 mg, 0.14 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (5.6 mg, 0.014 mmol) were reacted in toluene (4.7 mL) for 7 h. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, 40% Et_2O /hexanes) afforded compound **46f** (25.6 mg, 76%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 5.85 – 5.84 (m, 1H), 4.84 (s, 2H), 3.94 (t, $J = 5.4$ Hz, 2H), 2.80 – 2.78 (m, 1H), 2.63 – 2.60 (m, 2H), 1.21 (d, $J = 7.5$ Hz, 3H), 0.23 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 211.5, 177.1, 142.9, 139.8, 126.1, 73.0, 71.5, 46.2, 33.8, 15.3, –0.4 (3C); IR (thin film) 2958, 2925, 2869, 1687, 1528, 1250, 1193, 1136; HRMS (ES+) $\text{C}_{13}\text{H}_{21}\text{O}_2\text{Si}$ $[\text{M}+\text{H}^+]$ Calculated: 237.1311; Found: 237.1283; $[\alpha]_{\text{D}}^{20} = -1.6^\circ$ (c 1.6, CH_2Cl_2).

(R_a)-(3-(hexa-3,4-dien-1-yloxy)prop-1-yn-1-yl)benzene (18d)

Following the general procedure for preparation of allene-yne *via* Williamson etherification, (*R_a*)-hexa-3,4-dien-1-ol **26** (62.8 mg, 0.64 mmol) in THF (1.5 mL) was reacted with sodium hydride (51.2 mg, 60% dispersion in mineral oil, 1.27 mmol) and (3-bromoprop-1-yn-1-yl)benzene (187.2 mg, 0.96 mmol) for 3 h. Purification of the crude residue using a Biotage normal phase automated purification system (10 g SNAP column, gradient of 0 – 3% Et_2O /hexanes) afforded compound **18d** (85.2 mg, 63%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.46 – 7.45 (m, 2H), 7.32 – 7.30 (m, 3H), 5.12 – 5.08 (m, 2H), 4.38 (s, 2H), 3.65 (t, $J = 6.8$ Hz, 2H), 2.34 – 2.31 (m, 2H), 1.67 – 1.64 (m, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 205.3, 131.7 (2C), 128.3, 128.2 (2C), 122.7, 86.7, 86.0, 85.9, 85.3, 69.5, 58.8, 29.2, 14.4; IR (thin film) 3060, 2917, 2845, 1969, 1491, 1442, 1360, 1099; HRMS (ES+) $\text{C}_{15}\text{H}_{17}\text{O}$ $[\text{M}+\text{H}^+]$ Calculated: 213.1279; Found: 213.1280; $[\alpha]_{\text{D}}^{20} = -41.5^\circ$ (c 0.65, CH_2Cl_2).

(S)-6-Methyl-8-phenyl-3,4-dihydro-1H-cyclopenta[c]oxepin-7(6H)-one (46d)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **18d** (29.6 mg, 0.14 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (5.4 mg, 0.014 mmol) were reacted in toluene (4.4 mL) for 30 min. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, 45% Et_2O /hexanes) afforded compound **46d** (30 mg, 90%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.41 – 7.34 (m, 3H), 7.25 – 7.24 (m, 2H), 5.96 – 5.94 (m, 1H), 4.85 (s, 2H), 4.03 – 3.98 (m, 2H), 3.01 – 2.98 (m, 1H), 2.69 – 2.67 (m, 2H), 1.34 (d, $J = 7.5$ Hz, 3H); ^{13}C NMR (175 MHz, CDCl_3) δ 205.6, 164.4, 140.7, 139.1, 130.9, 129.3 (2C), 128.4, 128.3 (2C), 126.8, 71.9, 71.5, 45.3, 33.6, 15.5; IR (thin film) 2962, 2925, 2868, 1669, 1446, 1131; HRMS (ES+) $\text{C}_{16}\text{H}_{17}\text{O}_2$ $[\text{M}+\text{H}^+]$ Calculated: 241.1229; Found: 241.1204; $[\alpha]_{\text{D}}^{20} = -24^\circ$ (c 0.25, CH_2Cl_2).

(*R*_a)-N-(But-2-yn-1-yl)-N-(3-(dimethyl(phenyl)silyl)hexa-3,4-dien-1-yl)-4-methylbenzenesulfonamide (13c)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (*R*_a)-**22** (157 mg, 0.675 mmol) in THF (4.4 mL) was reacted with triphenylphosphine (213 mg, 0.81 mmol), *N*-(but-2-yn-1-yl)-4-methylbenzenesulfonamide³²**30c** (181 mg, 0.81 mmol) and diisopropylazodicarboxylate (160 μL , 0.81 mmol) for 3 h. Purification of the crude residue using a Biotage normal phase automated purification system (25 g SNAP column, gradient of 0 – 30% Et_2O /hexanes) afforded compound **13c** (272 mg, 92%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.65 (d, $J = 7.8$ Hz, 2H), 7.51 (d, $J = 7.6$ Hz, 2H), 7.38 – 7.32 (m, 3H), 7.24 (d, $J = 7.8$ Hz, 2H), 4.92 – 4.80 (m, 1H), 3.96 (d, $J = 2.5$ Hz, 2H), 3.22 – 3.10 (m, 2H), 2.41 (s, 3H), 2.16 (m, 2H), 1.63 (d, $J = 6.9$ Hz, 3H), 1.52 (t, $J = 2.5$ Hz, 3H), 0.36 (s, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 2078.0, 142.9, 137.9, 136.2, 133.7 (2C), 129.1 (2C), 129.0, 127.7 (2C), 127.7 (2C), 91.2, 81.2, 81.2, 72.0, 46.4, 37.1, 27.9, 21.4, 13.7, 3.2, –3.1, –3.2; IR (thin film) 3064, 2962, 2921, 2855, 2300, 2218, 1936, 1593, 1491; HRMS (ES+) $\text{C}_{25}\text{H}_{32}\text{NO}_2\text{SSi}$ $[\text{M}+\text{H}^+]$ Calculated: 438.1923; Found: 438.1926; $[\alpha]_{\text{D}}^{20} = +3.8^\circ$ (c 1.7, CH_2Cl_2).

(S)-5-(Dimethyl(phenyl)silyl)-6,8-dimethyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[c]azepin-7(6H)-one (35c)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **13c** (22.5 mg, 0.051 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (2 mg, 0.005 mmol) were reacted in toluene (1.6 mL) for 3 h. Purification of the crude residue by flash chromatography (55% Et_2O /hexanes) afforded the title compound **35c** (22.8 mg, 95%) as a yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.55 (d, $J = 8.1$ Hz, 2H), 7.40 – 7.34 (m, 5H), 7.22 (d, $J = 8.1$ Hz, 2H), 4.60 (d, $J = 17.0$ Hz, 1H), 4.46 (d, $J = 17.0$ Hz, 1H), 3.45 (t, $J = 6.1$ Hz, 2H), 2.56 – 2.51 (m, 3H), 2.40 (s, 3H), 1.89 (s, 3H), 0.91 (d, $J = 7.4$ Hz, 3H), 0.38 (s, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 208.4, 160.9, 153.9, 143.5, 138.3, 137.1, 136.4, 133.8 (2C), 133.3, 129.5, 129.4 (2C), 128.0 (2C), 127.1 (2C), 48.0, 43.8, 43.0, 29.7, 21.4, 18.4, 8.2, –1.3, –1.6; IR (thin film) 2978, 2925, 2872, 1703, 1605, 1466, 1344, 1258, 1160, 1102; HRMS (ES+) $\text{C}_{26}\text{H}_{31}\text{NO}_3\text{SSiNa}$ $[\text{M}+\text{Na}^+]$ Calculated: 488.1692; Found: 488.1708; $[\alpha]_{\text{D}}^{20} = +157^\circ$ (c 1.0, CH_2Cl_2).

(Z)-5-(dimethyl(phenyl)silyl)-3-ethylidene-1-tosyl-4-vinyl-2,3,6,7-tetrahydro-1H-azepine (36)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **13c** (32.5 mg, 0.074 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (1.4 mg, 0.004 mmol) were reacted in toluene (2.3 mL) for 7 h. Purification of the crude residue by flash chromatography (55% Et_2O /hexanes) afforded the cyclocarbonylation product **35** (14.4 mg,

42%) and triene **36** (15.6 mg, 48%) as yellow oils. ^1H NMR (300 MHz, CDCl_3) δ 7.63 (d, J = 8.3 Hz, 2H), 7.47 – 7.44 (m, 2H), 7.34 – 7.32 (m, 4H), 7.29 (s, 1H), 6.55 (dd, J = 16.9, 10.5 Hz, 1H), 5.52 – 5.45 (m, 1H), 5.15 (dd, J = 16.9, 1.9 Hz, 1H), 5.00 (dd, J = 10.5, 1.9 Hz, 1H), 3.82 (s, 2H), 3.07 – 3.03 (t, J = 5.9 Hz, 2H), 2.42 (s, 3H), 2.34 (t, J = 5.9 Hz, 2H), 1.78 (d, J = 7.0 Hz, 3H), 0.39 (s, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 153.7, 143.0, 138.9, 137.6, 135.7, 134.9, 133.9 (2C), 133.8, 129.6 (2C), 128.9, 127.9 (2C), 127.4 (2C), 127.3, 117.1, 46.6, 46.0, 31.7, 21.5, 13.3, –0.6 (2C); IR (thin film) 2966, 2921, 2847, 2010, 1515, 1462, 1429, 1336, 1254, 1160, 1103; HRMS (ES+) $\text{C}_{25}\text{H}_{32}\text{NO}_2\text{SSi}$ $[\text{M}+\text{H}^+]$ Calculated: 438.1923; Found: 438.1917.

(*R*_a)-*N*-(3-(Dimethyl(phenyl)silyl)hexa-3,4-dien-1-yl)-4-methyl-*N*-(prop-2-yn-1-yl)benzene sulfonamide (13e**)**

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (***R*_a-22**) (309 mg, 1.32 mmol) in THF (8.2 mL) was reacted with triphenylphosphine (415.4 mg, 1.58 mmol), 4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide³²**30e** (331 mg, 1.58 mmol) and diisopropylazodicarboxylate (274 μL , 1.58 mmol) for 2 h. Purification of the crude residue using a Biotage normal phase automated purification system (25 g SNAP column, gradient of 0 – 30% Et_2O /hexanes) afforded compound **13e** (500 mg, 90%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.65 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 7.0 Hz, 3H), 7.25 – 7.24 (m, 2H), 4.92 – 4.82 (m, 1H), 4.03 (d, J = 2.6 Hz, 2H), 3.22 – 3.18 (m, 2H), 2.42 (s, 3H), 2.18 – 2.15 (m, 2H), 1.96 (t, J = 2.5 Hz, 1H), 1.63 (d, J = 7.0 Hz, 3H), 0.36 (s, 6H); ^{13}C NMR (175 MHz, CD_2Cl_2) 208.0, 143.6, 138.0, 136.1, 133.8 (2C), 129.4 (2C), 129.1, 127.8 (2C), 127.5 (2C), 91.2, 81.4, 76.9, 73.3, 46.5, 36.6, 27.9, 21.3, 13.5, –3.3, –3.4; IR (thin film) 3289, 2962, 2917, 2860, 1936, 1597, 1495, 1450, 1348; HRMS (ES+) $\text{C}_{24}\text{H}_{30}\text{NO}_2\text{SSi}$ $[\text{M}+\text{H}^+]$ Calculated: 424.1767; Found: 424.1797; $[\alpha]_{\text{D}}^{20}$ = +3.8° (c 1.65, CH_2Cl_2).

(*S*)-5-(Dimethyl(phenyl)silyl)-6-methyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[*c*] azepin-7(6*H*)-one (35e**)**

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **13e** (41 mg, 0.097 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (4.2 mg, 0.009 mmol) were reacted in toluene (3 mL) for 2.5 h. Purification of the crude residue by flash chromatography (65% Et_2O /hexanes) afforded the cyclocarbonylation product **35e** (28.9 mg, 66%) and triene **49** (6.1 mg, 13%) as yellow oils. ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, J = 8.3 Hz, 2H), 7.39 – 7.35 (m, 5H), 7.34 – 7.24 (m, 2H), 6.04 (s, 1H), 4.54 (q, J = 16.9 Hz, 2H), 3.43 – 3.41 (m, 2H), 2.59 – 2.54 (m, 3H), 2.40 (s, 3H), 0.93 (d, J = 7.5 Hz, 3H), 0.39 (s, 6H); ^{13}C NMR (175 MHz, CDCl_3) 208.3, 167.4, 154.1, 143.6, 137.6, 136.7, 136.1, 133.8 (2C), 130.6, 129.7, 129.5 (2C), 128.1 (2C), 127.3 (2C), 47.8, 45.3, 45.3, 29.8, 21.5, 18.4, –1.5, –1.8; IR (thin film) 3056, 2974, 2925, 2868, 2014, 1699, 1573, 1462, 1340, 1164; HRMS (ES+) $\text{C}_{25}\text{H}_{30}\text{NO}_3\text{SSi}$ $[\text{M}+\text{H}^+]$ Calculated: 452.1716; Found: 452.1693; $[\alpha]_{\text{D}}^{20}$ = +100.4° (c 2.5, CH_2Cl_2).

5-(Dimethyl(phenyl)silyl)-3-methylene-1-tosyl-4-vinyl-2,3,6,7-tetrahydro-1*H*-azepine (49**)**

^1H NMR (300 MHz, CDCl_3) δ 7.63 (d, J = 8.2 Hz, 2H), 7.50 – 7.44 (m, 2H), 7.35 – 7.33 (m, 3H), 7.29 – 7.26 (m, 2H), 6.55 (dd, J = 16.9, 10.5 Hz, 1H), 5.37 (d, J = 1.5 Hz, 1H), 5.26 – 5.16 (m, 1H), 5.03 (dd, J = 10.5, 1.7 Hz, 1H), 4.99 (s, 1H), 3.88 (s, 2H), 3.13 (t, J = 6.1 Hz, 2H), 2.41 – 2.36 (m, 5H), 0.40 (s, 6H); ^{13}C NMR (175 MHz, CDCl_3) δ 151.9, 143.4, 143.0, 138.6, 136.9, 136.0, 135.3, 133.8 (2C), 129.5 (2C), 129.0, 127.9 (2C), 127.3 (2C), 117.1, 117.1, 51.1, 45.2, 31.8, 21.4, –0.7 (2C); IR (thin film) 3060, 2962, 2921, 2847, 1343, 1164, 1106; HRMS (ES+) $\text{C}_{24}\text{H}_{30}\text{NO}_2\text{SSi}$ $[\text{M}+\text{H}^+]$ Calculated: 424.1767; Found: 424.1787;

(*R_a*)-*N*-(3-(Dimethyl(phenyl)silyl)hexa-3,4-dien-1-yl)-4-methyl-*N*-(3-(trimethylsilyl) prop-2-yn-1-yl)benzenesulfonamide (13f)

Following the general procedure for preparation of allene-yne *via* silylation of the terminal alkyne, allene-yne **13e** (92 mg, 0.22 mmol) in THF (2 mL) was reacted with lithium hexamethyldisilylamide (0.28 mL, 1 M in THF, 0.28 mmol) and trimethylsilyl chloride (55 μ L, 0.434 mmol). Purification of the crude residue by silica gel chromatography using 10% Et₂O/hexanes to afford compound **13f** (93.3 mg, 87%) as a clear yellow oil. ¹H NMR (600 MHz, CDCl₃) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.52 (dd, *J* = 7.4, 2.0 Hz, 2H), 7.38 – 7.35 (m, 3H), 7.25 – 7.23 (d, *J* = 8.3 Hz, 2H), 4.87 (m, 1H), 4.05 (s, 2H), 3.22 – 3.18 (m, 2H), 2.40 (s, 3H), 2.19 – 2.16 (m, 2H), 1.63 (d, *J* = 7.0 Hz, 3H), 0.36 (d, *J* = 1.3 Hz, 6H), –0.02 (s, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 208.0, 143.1, 137.9, 136.1, 133.8 (2C), 129.4 (2C), 129.1, 127.8 (2C), 127.6 (2C), 98.2, 91.2, 90.6, 81.3, 46.3, 37.4, 27.8, 21.45, 13.7, –0.5 (3C), –3.0, –3.1; IR (thin film) 3064, 2958, 2913, 2173, 1940, 1601, 1348; HRMS (ES+) C₂₇H₃₈NO₂SSi₂ [M+H⁺] Calculated: 496.2162; Found: 496.2152; [α]_D²⁰ = +1.2° (c 1.65, CH₂Cl₂).

(*S*)-5-(Dimethyl(phenyl)silyl)-6-methyl-2-tosyl-8-(trimethylsilyl)-1,2,3,4-tetrahydro cyclopenta[*c*]azepin-7(6*H*)-one (35f)

Following the General Procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **13f** (25 mg, 0.050 mmol) and [Rh(CO)₂Cl]₂ (2 mg, 0.005 mmol) were reacted in toluene (1.6 mL) for 3 h. Purification of the crude residue by flash chromatography (55% Et₂O/hexanes) afforded the title compound **35f** (23.4 mg, 89%) as a yellow oil. ¹H NMR (300 MHz, CDCl₃) δ 7.58 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.33 (m, 6H), 7.23 (s, 1H), 4.65 (d, *J* = 17.2 Hz, 1H), 4.56 (d, *J* = 17.2 Hz, 1H), 3.48 – 3.31 (m, 2H), 2.61 – 2.48 (m, 3H), 2.40 (s, 3H), 0.89 (d, *J* = 7.4 Hz, 3H), 0.36 (d, *J* = 9.0 Hz, 15H); ¹³C NMR (175 MHz, CDCl₃) δ 212.5, 174.1, 156.1, 143.4, 142.1, 137.1, 136.5, 134.3, 133.9 (2C), 129.5 (3C), 128.0 (2C), 127.2 (2C), 47.3, 45.5, 45.1, 29.7, 21.5, 18.8, –0.5 (3C), –1.23, –1.6; IR (thin film) 3060, 2962, 2921, 2855, 2247, 1932, 1691, 1601, 1544, 1462, 1352, 1254, 1164; HRMS (ES+) C₂₈H₃₈NO₂SSi₂ [M+H⁺] Calculated: 524.2111; Found: 524.2101; [α]_D²⁰ = +70.4° (c 0.75, CH₂Cl₂).

(*R_a*)-*N*-(3-(dimethyl(phenyl)silyl)hexa-3,4-dien-1-yl)-4-methyl-*N*-(3-phenylprop-2-yn-1-yl) benzenesulfonamide (13d)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (*R_a*)-**22** (93.6 mg, 0.402 mmol) in THF (2.8 mL) was reacted with triphenylphosphine (127 mg, 0.48 mmol), 4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide³² **30d** (134 mg, 0.48 mmol) and diisopropylazodicarboxylate (95 μ L, 0.48 mmol) for 3 h. Purification of the crude residue using a Biotage normal phase automated purification system (25 g SNAP column, gradient of 0 – 30% Et₂O/hexanes) afforded compound **13d** (185 mg, 92%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.52 – 7.49 (m, 2H), 7.35 – 7.32 (m, 4H), 7.23 – 7.19 (m, 3H), 7.04 (dd, *J* = 8.0, 1.7 Hz, 2H), 4.90 – 4.86 (m, 1H), 4.24 (s, 2H), 3.29 – 3.23 (m, 2H), 2.33 (s, 3H), 2.23 (td, *J* = 8.1, 2.7 Hz, 2H), 1.63 (d, *J* = 7.0 Hz, 3H), 0.36 (d, *J* = 0.8 Hz, 6H); ¹³C NMR (175 MHz, CDCl₃) δ 208.0, 143.2, 137.9, 136.0, 133.7 (2C), 131.4 (2C), 129.4 (2C), 129.1, 128.3, 128.0 (2C), 127.8 (2C), 127.6 (2C), 122.2, 91.2, 85.4, 82.0, 81.3, 46.5, 37.4, 27.9, 21.4, 13.7, –3.1, –3.1; IR (thin film) 3068, 2953, 2921, 2855, 2238, 1940, 1589, 1486; HRMS (ES+) C₃₀H₃₄NO₂SSi₂ [M+H⁺] Calculated: 500.2080; Found: 500.2086; [α]_D²⁰ = +8.7° (c 1.15, CH₂Cl₂).

(S)-5-(Dimethyl(phenyl)silyl)-6-methyl-8-phenyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[c]azepin-7(6H)-one (35d)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **13d** (41.5 mg, 0.083 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (3.2 mg, 0.003 mmol) were reacted in toluene (2.5 mL) for 3 h. Purification of the crude residue by flash chromatography (55% Et_2O /hexanes) afforded the title compound **35d** (40.1 mg, 92%) as a yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.49 – 7.32 (m, 12H), 7.21 (d, J = 8.0 Hz, 2H), 4.63 (s, 2H), 3.51 (t, J = 6.1 Hz, 2H), 2.71 (q, J = 7.3 Hz, 1H), 2.65 – 2.58 (t, J = 5.4 Hz, 2H), 2.40 (s, 3H), 0.97 (t, J = 8.4 Hz, 3H), 0.45 (s, 6H); ^{13}C NMR (175 MHz, CDCl_3) δ 206.4, 161.4, 153.7, 143.4, 140.7, 137.0, 136.6, 135.7, 133.9 (2C), 129.9, 129.6 (3C), 129.4 (2C), 128.9, 128.6 (2C), 128.1 (2C), 127.1 (2C), 48.2, 44.6, 43.7, 29.8, 21.5, 18.7, –1.2, –1.5; IR (thin film) 2970, 2917, 2859, 2018, 1736, 1707, 1454, 1340, 1164; HRMS (ES+) $\text{C}_{31}\text{H}_{34}\text{NO}_3\text{SSi}$ $[\text{M}+\text{H}^+]$ Calculated: 528.2029; Found: 528.2034; $[\alpha]_{\text{D}}^{20}$ = +192° (c 0.75, CH_2Cl_2).

4-Methyl-N-(3-(thiophen-3-yl)prop-2-yn-1-yl)benzenesulfonamide (30a)

A mixture of propargyltosylamide (444 mg, 1.97 mmol), 3-bromothiophene (963 mg, 5.91 mmol), palladium dichloride bistrisphenylphosphine (27.7 mg, 0.039 mmol), copper iodide (15 mg, 0.079 mmol) in piperidine (3.9 mL) were heated at 80 °C for 17 h. The solution was concentrated under reduced pressure. Purification of the crude residue using a Biotage normal phase automated purification system (25 g SNAP column, gradient of 5 – 25% EtOAc /hexanes) afforded compound **30a** (155.6 mg, 27%) as a white foam. ^1H NMR (600 MHz, CDCl_3) δ 7.81 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 7.24 – 7.15 (m, 2H), 6.84 (d, J = 4.4 Hz, 1H), 4.69 – 4.65 (m, 1H), 4.05 (d, J = 6.1 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 143.7, 136.8, 129.6 (2C), 129.5, 129.1, 127.5 (2C), 125.2, 121.1, 82.8, 79.9, 33.8, 21.5; IR (thin film) 3265, 1593, 1430, 1324, 1156, 1091, 1042, 813, 788; HRMS (ES+) $\text{C}_{14}\text{H}_{12}\text{NO}_2\text{S}_2$ $[\text{M}+\text{H}^+]$ Calculated: 290.0276; Found: 290.0299.

(*R*_a)-N-(3-(Dimethyl(phenyl)silyl)hexa-3,4-dien-1-yl)-4-methyl-N-(3-(thiophen-3-yl)prop-2-yn-1-yl)benzenesulfonamide (13a)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (***R*_a**-**22**) (39.8 mg, 0.171 mmol) in THF (1.2 mL) was reacted with triphenylphosphine (54 mg, 0.21 mmol), 4-methyl-N-(3-(thiophen-3-yl)prop-2-yn-1-yl)benzenesulfonamide **30a** (60 mg, 0.21 mmol) and diisopropylazodicarboxylate (41 μL , 0.21 mmol) for 10 h. Purification of the crude residue using a Biotage normal phase automated purification system (10 g SNAP column, gradient of 2 – 4% EtOAc /hexanes) afforded compound **13a** (77.6 mg, 90%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.67 (d, J = 8.3 Hz, 2H), 7.51 (dd, J = 7.8, 1.7 Hz, 2H), 7.37 – 7.34 (m, 3H), 7.22 – 7.19 (m, 3H), 7.09 (dd, J = 3.0, 1.1 Hz, 1H), 6.76 (dd, J = 5.0, 1.2 Hz, 1H), 4.90 – 4.86 (m, 1H), 4.22 (d, J = 1.6 Hz, 2H), 3.24 (dd, J = 8.9, 6.9 Hz, 2H), 2.35 (s, 3H), 2.23 – 2.20 (m, 2H), 1.63 (d, J = 7.0 Hz, 3H), 0.36 (d, J = 2.0 Hz, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 208.0, 143.2, 137.9, 136.1, 133.8 (2C), 129.6, 129.4 (2C), 129.1, 128.7, 127.8 (2C), 127.7 (2C), 125.1, 121.3, 91.2, 81.7, 81.4, 80.5, 46.6, 37.4, 28.0, 21.5, 13.7, –3.0 (2C); IR (thin film) 3109, 2958, 2921, 2864, 1936, 1732, 1593, 1458, 1434, 1352, 1164, 1111; HRMS (ES+) $\text{C}_{28}\text{H}_{31}\text{NO}_2\text{NaS}_2\text{Si}$ $[\text{M}+\text{Na}^+]$ Calculated: 528.1463; Found: 528.1414; $[\alpha]_{\text{D}}^{20}$ = +4° (c 1.75, CH_2Cl_2).

(S)-5-(Dimethyl(phenyl)silyl)-6-methyl-8-(thiophen-3-yl)-2-tosyl-1,2,3,4-tetrahydrocyclopenta[c]azepin-7(6H)-one (35a)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **13a** (17.8 mg, 0.036 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (1.4 mg, 0.003 mmol) were reacted in toluene (1.2 mL) for 2.5 h. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, gradient of 5 – 25% EtOAc/hexanes) afforded compound **35a** (13.5 mg, 72%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.68 – 7.66 (m, 1H), 7.47 – 7.42 (m, 5H), 7.39 – 7.33 (m, 4H), 7.22 (d, J = 8.0 Hz, 2H), 4.73 (s, 2H), 3.52 (t, J = 6.1 Hz, 2H), 2.68 – 2.58 (m, 3H), 2.40 (s, 3H), 0.98 (d, J = 7.4 Hz, 3H), 0.43 (d, J = 1.3 Hz, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 206.4, 159.9, 153.8, 143.5, 137.1, 136.5, 135.6, 135.5, 133.9 (2C), 130.4, 129.6, 129.4 (2C), 128.1 (2C), 127.9, 127.1 (2C), 126.8, 125.9, 48.3, 44.5, 43.8, 29.9, 21.5, 18.8, –1.2, –1.5; IR (thin film) 2958, 2925, 1695, 1605, 1467, 1430, 1344, 1246, 1160, 1107, 964; HRMS (ES+) $\text{C}_{29}\text{H}_{31}\text{NO}_3\text{NaS}_2\text{Si}$ $[\text{M}+\text{Na}^+]$ Calculated: 556.1412; Found: 556.1465; $[\alpha]_{\text{D}}^{20}$ = +174° (c 1.15, CH_2Cl_2).

4-Methyl-N-(3-(thiophen-2-yl)prop-2-yn-1-yl)benzenesulfonamide (30b)

A mixture of propargyltosylamide (415.9 mg, 1.84 mmol), 2-iodothiophene (215 μL , 2.03 mmol), palladium dichloride bistrisphenylphosphine (25.9 mg, 0.037 mmol), copper iodide (14.1 mg, 0.074 mmol) and triethylamine (1.29 mL, 0.092 mmol) in acetonitrile (3 mL) was stirred at rt for 19 h. The residue obtained after removal of acetonitrile was taken up in CH_2Cl_2 (30 mL) and washed with water (10 mL). The organic phase was separated, dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification of the crude residue by silica gel column chromatography (Hex/ Et_2O 50%), afforded compound **30b** (316 mg, 59%) as a white foam. ^1H NMR (300 MHz, CDCl_3) δ 7.80 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.21 (dd, J = 5.1, 1.2 Hz, 1H), 6.97 (d, J = 3.6 Hz, 1H), 6.92 – 6.89 (m, 1H), 4.63 – 4.62 (m, 1H), 4.09 (d, J = 6.2 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 143.9, 136.6, 132.4, 129.7 (2C), 127.4 (2C), 126.8, 121.9, 87.1, 78.1, 33.9, 21.6; IR (thin film) 3265, 2361, 1589, 1491, 1422, 1344, 1315, 1160, 1091, 1038, 845; HRMS (ES+) $\text{C}_{14}\text{H}_{12}\text{NO}_2\text{S}_2$ $[\text{M}-\text{H}^+]$ Calculated: 290.0309; Found: 290.0316.

(R_a)-N-(3-(dimethyl(phenyl)silyl)hexa-3,4-dien-1-yl)-4-methyl-N-(3-(thiophen-2-yl) prop-2-yn-1-yl)benzenesulfonamide (13b)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (**R_a**)-**22** (35.2 mg, 0.151 mmol) in THF (1.0 mL) was reacted with triphenylphosphine (48 mg, 0.18 mmol), 4-methyl-N-(3-(thiophen-2-yl)prop-2-yn-1-yl)benzenesulfonamide **30b** (53 mg, 0.18 mmol) and diisopropylazodicarboxylate (36 μL , 0.18 mmol) for 11 h. Purification of the crude residue using a Biotage normal phase automated purification system (10 g SNAP column, gradient of 2 – 4% EtOAc/hexanes) afforded compound **13b** (69.3 mg, 90%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.67 (d, J = 8.0 Hz, 2H), 7.52 – 7.50 (m, 2H), 7.36 – 7.33 (m, 3H), 7.24 – 7.20 (m, 3H), 6.90 (d, J = 3.3 Hz, 2H), 4.90 – 4.86 (m, 1H), 4.25 (s, 2H), 3.25 – 3.20 (m, 2H), 2.36 (s, 3H), 2.24 – 2.18 (m, 2H), 1.63 (d, J = 7.0 Hz, 3H), 0.36 (s, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 208.0, 143.3, 137.9, 135.8, 133.8 (2C), 132.1, 129.5 (2C), 129.1, 127.8 (2C), 127.6 (2C), 127.2, 126.7, 122.2, 91.2, 86.1, 81.4, 78.6, 46.5, 37.5, 27.9, 21.5, 13.7, –3.1 (2C); IR (thin film) 2954, 2925, 2852, 2353, 2329, 1936, 1593, 1430, 1352, 1250, 1185, 1168, 1107; HRMS (ES+) $\text{C}_{28}\text{H}_{31}\text{NO}_2\text{NaS}_2\text{Si}$ $[\text{M}+\text{H}^+]$ Calculated: 528.1463; Found: 528.1494; $[\alpha]_{\text{D}}^{20}$ = +2° (c 1.8, CH_2Cl_2).

(S)-5-(Dimethyl(phenyl)silyl)-6-methyl-8-(thiophen-2-yl)-2-tosyl-1,2,3,4-tetrahydrocyclopenta[c]azepin-7(6H)-one (35b)

Following the General Procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **13b** (28.3 mg, 0.056 mmol) and [Rh(CO)₂Cl]₂ (2.2 mg, 0.006 mmol) were reacted in toluene (1.8 mL) for 3 h. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, gradient of 5 – 25% EtOAc/hexanes) afforded compound **35b** (24.9 mg, 84%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 7.56 (d, *J* = 5.2 Hz, 2H), 7.45 – 7.35 (m, 8H), 7.21 – 7.19 (m, 3H), 4.89 – 4.82 (m, 2H), 3.55 – 3.53 (m, 2H), 2.63 – 2.60 (m, 2H), 2.39 (s, 3H), 0.95 (d, *J* = 7.4 Hz, 3H), 0.43 (d, *J* = 5.6 Hz, 6H); ¹³C NMR (150 MHz, CDCl₃) δ 205.3, 158.9, 153.5, 143.5, 136.9, 136.5, 135.8, 133.9 (2C), 133.7, 130.9, 129.6, 129.4 (2C), 129.2, 129.0, 128.1 (2C), 127.4, 127.0 (2C), 48.6, 44.3, 43.9, 30.0, 21.5, 18.8, –1.2, –1.5; IR (thin film) 3060, 2954, 2929, 2872, 1704, 1589, 1434, 1344, 1246, 1152, 1103, 1017; HRMS (ES+) C₂₉H₃₀NO₃S₂Si [M–H⁺] Calculated: 532.1436; Found: 532.1453; [α]_D²⁰ = +188° (c 1.80, CH₂Cl₂).

tert-Butyl (3-cyclopropylprop-2-yn-1-yl)(tosyl)carbamate (50)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, 3-cyclopropylprop-2-yn-1-ol (283 mg, 2.94 mmol) in THF (21 mL) was reacted with triphenylphosphine (927 mg, 3.53 mmol), *tert*-butyl tosylcarbamate (959 mg, 3.53 mmol) and diisopropylazodicarboxylate (0.7 mL, 3.53 mmol) for 11 h. Purification of the crude residue by silica gel chromatography using 20% Et₂O/hexanes afforded compound **50** (535 mg, 52%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.28 (m, 2H), 4.57 (d, *J* = 2.0 Hz, 2H), 2.45 (s, 3H), 1.34 (s, 9H), 1.27 – 1.23 (m, 1H), 0.78 – 0.74 (m, 2H), 0.67 – 0.64 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 150.3, 144.2, 136.9, 129.0 (2C), 128.2 (2C), 87.5, 84.5, 70.5, 36.4, 27.8 (3C), 21.6, 7.9 (2C), –0.6; IR (thin film) 2974, 2925, 2251, 2235, 1724, 1597, 1356, 1311, 1279, 1091, 1070; HRMS (ES+) C₁₄H₁₆NO₄S [M–C₅H₁₀O₂+H] Calculated: 294.0800; Found: 294.0810.

N-(3-Cyclopropylprop-2-yn-1-yl)-4-methylbenzenesulfonamide (30g)

To a solution of *tert*-butyl (3-cyclopropylprop-2-yn-1-yl)(tosyl)carbamate **50** (102.7 mg, 0.293 mmol) in methanol (1.7 mL) and THF (0.7 mL) was added lithium hydroxide (88 mg, 1.17 mmol). After stirring for 12 h at rt, the mixture was diluted with CH₂Cl₂ (40 mL) and HCl 1 M (10 mL). The organic layer was separated, washed with brine (10 mL) and dried (Na₂SO₄). The solvent was removed under reduced pressure. Purification of the crude residue by silica gel chromatography using 40% Et₂O/hexanes afforded compound **30g** (52.3 mg, 71%) as a white foam. ¹H NMR (300 MHz, CDCl₃) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.55 (br. s, 1H), 3.76 – 3.76 (m, 2H), 2.43 (s, 3H), 1.03 (m, 1H), 0.65 – 0.62 (m, 2H), 0.42 – 0.40 (m, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 143.5, 136.8, 129.5 (2C), 127.4 (2C), 88.4, 69.3, 33.4, 21.5, 7.8 (2C), –0.9; IR (thin film) 3265, 1438, 1315, 1160, 1095, 1058, 1030; HRMS (ES+) C₁₃H₁₆NO₂S [M+H⁺] Calculated: 250.0902; Found: 250.0888.

(R_a)-N-(3-Cyclopropylprop-2-yn-1-yl)-N-(3-(dimethyl(phenyl)silyl)hexa-3,4-dien-1-yl)-4-methylbenzenesulfonamide (13g)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (*R_a*)-**22** (45 mg, 0.19 mmol) in THF (1.4 mL) was reacted with triphenylphosphine (61.1 mg, 0.23 mmol), *N*-(3-cyclopropylprop-2-yn-1-yl)-4-methylbenzenesulfonamide **30g** (58.3 mg, 0.23 mmol) and diisopropylazodicarboxylate (46 μL, 0.23 mmol) for 11 h. Purification of the crude residue using a Biotage normal phase automated purification system (12 g SNAP column, gradient of 1 – 7% EtOAc/hexanes) afforded compound **13g**

(63.7 mg, 73%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.66 (d, J = 8.3 Hz, 2H), 7.56 – 7.54 (m, 2H), 7.40 – 7.38 (m, 3H), 7.29 – 7.27 (dd, J = 8.8, 1.2 Hz, 2H), 4.92 – 4.89 (m, 1H), 4.00 (d, J = 2.0 Hz, 2H), 3.22 – 3.18 (m, 2H), 2.45 (s, 3H), 2.21 – 2.16 (m, 2H), 1.67 (d, J = 7.0 Hz, 3H), 1.00 – 0.96 (m, 1H), 0.65 – 0.61 (m, 2H), 0.40 (d, J = 1.0 Hz, 6H), 0.33 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 208.0, 142.9, 137.9, 136.3, 133.8 (2C), 129.2 (2C), 129.1, 127.8 (2C), 127.6 (2C), 91.3, 88.9, 81.2, 67.9, 46.3, 37.0, 27.9, 21.5, 13.7, 7.8 (2C), –0.9, –3.0, –3.1; IR (thin film) 2954, 2921, 2251, 1932, 1601, 1454, 1430, 1348, 1254, 1164, 1107, 1030; HRMS (ES+) $\text{C}_{27}\text{H}_{34}\text{NO}_2\text{SSi}$ [$\text{M}+\text{H}^+$] Calculated: 464.2080; Found: 464.2053; $[\alpha]_{\text{D}}^{20}$ = +5.7° (c 0.70, CH_2Cl_2).

(S)-8-Cyclopropyl-5-(dimethyl(phenyl)silyl)-6-methyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[c]azepin-7(6H)-one (35g)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **13g** (24.5 mg, 0.053 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (2.1 mg, 0.0053 mmol) were reacted in toluene (1.8 mL) for 135 min. Purification of the crude residue by silica gel chromatography using 40% Et_2O /hexanes afforded compound **35g** (22.1 mg, 83%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.62 (d, J = 8.0 Hz, 2H), 7.36 – 7.32 (m, 5H), 7.25 – 7.21 (m, 2H), 4.65 – 4.64 (m, 2H), 3.43 – 3.43 (m, 2H), 2.55 – 2.51 (m, J = 4.8 Hz, 2H), 2.41 – 2.38 (m, 4H), 1.62 – 1.57 (m, 1H), 1.30 – 1.25 (m, 2H), 0.93 – 0.90 (m, 2H), 0.81 (d, J = 7.4 Hz, 3H), 0.36 – 0.35 (t, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 207.5, 160.6, 153.2, 143.4, 141.4, 137.2, 136.3, 133.8 (2C), 132.2, 129.5, 129.3 (2C), 127.9 (2C), 127.3 (2C), 48.1, 44.3, 42.5, 29.5, 21.5, 18.4, 8.1, 6.1, 6.0, –1.2, –1.5; IR (thin film) 2962, 2925, 2868, 2018, 1695, 1589, 1467, 1348, 1250, 1160, 1103; HRMS (ES+) $\text{C}_{28}\text{H}_{34}\text{NO}_3\text{SSi}$ [$\text{M}+\text{H}^+$] Calculated: 492.2029; Found: 492.2042; $[\alpha]_{\text{D}}^{20}$ = +113.8° (c 1.45, CH_2Cl_2).

(R_a)-N-(Hexa-3,4-dien-1-yl)-4-methyl-N-(3-phenylprop-2-yn-1-yl)benzene sulfonamide (14d)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (**R_a**)-**29** (45 mg, 0.21 mmol) in THF (1.5 mL) was reacted with triphenylphosphine (65.5 mg, 0.25 mmol), 4-methyl-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide³⁰**30d** (71.2 mg, 0.25 mmol) and diisopropylazodicarboxylate (49 μL , 0.25 mmol) for 11 h. Purification of the crude residue by silica gel chromatography using 1% Et_2O /hexanes afforded compound **14d** (80.2 mg, 92%) as a colorless oil. ^1H NMR (700 MHz, CDCl_3) δ 7.70 (d, J = 8.3 Hz, 2H), 7.27 – 7.25 (m, 5H), 7.20 – 7.16 (m, 5H), 7.00 (d, J = 7.0 Hz, 2H), 6.15 – 6.13 (m, 1H), 4.34 (d, J = 18.5 Hz, 2H), 4.27 (d, J = 18.5 Hz, 2H), 3.47 – 3.43 (m, 1H), 3.34 – 3.30 (m, 1H), 2.44 – 2.41 (m, 2H), 2.29 (s, 3H), 2.15 – 2.09 (m, 2H), 1.45 – 1.44 (m, 1H), 1.35 – 1.32 (m, 2H), 0.86 (t, J = 7.3 Hz, 3H); ^{13}C NMR (175 MHz, CDCl_3) δ 202.3, 143.4, 135.6, 135.4, 131.4 (2C), 129.4 (2C), 128.6 (2C), 128.3, 128.1 (2C), 127.7 (2C), 126.6, 126.5 (2C), 122.1, 105.4, 96.0, 85.7, 81.6, 44.8, 37.31, 32.1, 31.2, 29.7, 22.4, 21.4, 13.9; IR (thin film) 2958, 2925, 2855, 1597, 1495, 1458, 1352, 1160, 1095, 918; HRMS (ES+) $\text{C}_{31}\text{H}_{34}\text{NO}_2\text{S}$ [$\text{M}+\text{H}^+$] Calculated: 484.2310; Found: 484.2283; $[\alpha]_{\text{D}}^{20}$ = –54.3° (c 1.15, CH_2Cl_2).

(S)-6-Methyl-8-phenyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[c]azepin-7(6H)-one (42d)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **14d** (22.7 mg, 0.054 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (2.1 mg, 0.0054 mmol) were reacted in toluene (1.7 mL) for 30 min. Purification of the crude residue by silica gel chromatography using 60% Et_2O /hexanes afforded compound **42d** (21.6 mg, 76%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.50 – 7.32 (m, 7H), 7.24 – 7.20 (m, 5H), 6.96 – 6.93 (m, 2H), 4.83 (d, J = 16.9 Hz, 1H), 4.61 (d, J = 16.8 Hz, 1H), 3.91 (s, 1H), 3.72 – 3.65 (m, 2H), 2.76 – 2.71 (m, 1H), 2.59 – 2.50 (m, 1H), 2.41 (s, 3H), 1.93 – 1.87 (m, 2H),

1.02 – 0.98 (m, 2H), 0.88 – 0.86 (m, 2H), 0.69 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 201.8, 162.8, 143.5, 141.4, 139.4, 137.8, 136.8, 136.0, 130.3, 129.6 (2C), 129.5 (2C), 128.7 (2C), 128.6, 128.5 (2C), 127.6 (2C), 127.2 (2C), 126.9, 55.4, 47.9, 44.3, 37.1, 31.1, 29.2, 22.7, 21.6, 13.7; IR (thin film) 2954, 2929, 2864, 1699, 1499, 1339, 1164, 1095; HRMS (ES+) $\text{C}_{32}\text{H}_{34}\text{NO}_3\text{S}$ [$\text{M}+\text{H}^+$] Calculated: 512.2259; Found: 512.2232; $[\alpha]_{\text{D}}^{20} = +61.1^\circ$ (c 0.90, CH_2Cl_2).

(*R*_a)-*N*-(Hexa-3,4-dien-1-yl)-4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzene sulfonamide (14c)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (*R*_a)-**29** (50.7 mg, 0.23 mmol) in THF (1.7 mL) was reacted with triphenylphosphine (74 mg, 0.28 mmol), *N*-(but-2-yn-1-yl)-4-methylbenzenesulfonamide³⁰ (63 mg, 0.28 mmol) and diisopropylazodicarboxylate (56 μL , 0.28 mmol) for 12 h. Purification of the crude residue by silica gel chromatography using 10% Et_2O /hexanes afforded compound **14c** (91.9 mg, 93%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.69 – 7.68 (d, $J = 8.3$ Hz, 2H), 7.30 – 7.26 (m, 4H), 7.23 – 7.22 (m, 3H), 6.14 (t, $J = 2.9$ Hz, 1H), 4.08 – 3.99 (m, 2H), 3.36 – 3.32 (m, 1H), 3.28 – 3.23 (m, 1H), 2.39 (s, 3H), 2.37 – 2.36 (m, 2H), 2.13 – 2.07 (m, 2H), 1.51 (t, $J = 2.4$ Hz, 3H), 1.46 – 1.43 (m, 2H), 1.37 – 1.33 (m, 2H), 0.88 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 202.2, 143.1, 135.9, 135.5, 129.2 (2C), 128.5 (2C), 127.7 (2C), 126.6, 126.5 (2C), 105.4, 95.9, 81.5, 71.7, 44.7, 37.0, 32.1, 31.2, 29.7, 22.4, 21.5, 13.9, 3.2; IR (thin film) 2954, 2925, 2864, 1593, 1499, 1458, 1344, 1164, 1091, 915; HRMS (ES+) $\text{C}_{26}\text{H}_{32}\text{NO}_2\text{S}$ [$\text{M}+\text{H}^+$] Calculated: 422.2154; Found: 422.2120; $[\alpha]_{\text{D}}^{20} = -43.5^\circ$ (c 1.15, CH_2Cl_2).

(*S*)-5-Butyl-8-methyl-6-phenyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[*c*]azepin-7(6*H*)-one (42c)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **14c** (33.5 mg, 0.079 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (3.1 mg, 0.0079 mmol) were reacted in toluene (2.5 mL) for 90 min. Purification of the crude residue using a Biotage normal phase automated purification system (12 g SNAP column, gradient of 5 – 30% EtOAc /hexanes) afforded compound **42c** (29.1 mg, 82%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.68 (d, $J = 8.2$ Hz, 2H), 7.29 (d, $J = 8.1$ Hz, 2H), 7.19 – 7.18 (m, 3H), 6.89 – 6.88 (m, 2H), 4.67 (d, $J = 16.9$ Hz, 1H), 4.50 (d, $J = 16.9$ Hz, 1H), 3.77 (s, 1H), 3.61 – 3.60 (m, 2H), 2.61 – 2.53 (m, 2H), 2.42 (s, 3H), 1.86 (s, 3H), 1.83 – 1.78 (m, 2H), 1.12 – 1.10 (m, 1H), 1.02 – 0.95 (m, 2H), 0.84 – 0.83 (m, 1H), 0.67 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 203.6, 162.3, 143.7, 139.2, 137.9, 136.4, 136.3, 135.9, 129.7 (2C), 128.6 (2C), 127.5 (2C), 127.1 (2C), 126.8, 54.9, 47.8, 44.6, 36.9, 31.8, 29.3, 22.6, 21.6, 13.7, 8.6; IR (thin film) 2954, 2925, 2860, 2361, 2333, 1699, 1597, 1487, 1454, 1344, 1266, 1152, 1095; HRMS (ES+) $\text{C}_{27}\text{H}_{32}\text{NO}_3\text{S}$ [$\text{M}+\text{H}^+$] Calculated: 450.2103; Found: 450.2058; $[\alpha]_{\text{D}}^{20} = +112.2^\circ$ (c 0.90, CH_2Cl_2).

(*R*_a)-4-Methyl-*N*-(3-(2-phenylvinylidene)heptyl)-*N*-(prop-2-yn-1-yl)benzene sulfonamide (14e)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (*R*_a)-**29** (114.4 mg, 0.53 mmol) in THF (3.8 mL) was reacted with triphenylphosphine (166 mg, 0.63 mmol), 4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide³⁰ **30e** (133 mg, 0.63 mmol) and diisopropylazodicarboxylate (125 μL , 0.63 mmol) for 12 h. Purification of the crude residue using a Biotage normal phase automated purification system (25 g SNAP column, gradient of 0 – 7% EtOAc /hexanes) afforded compound **14e** (182.1 mg, 85%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.66 (d, $J = 8.1$ Hz, 2H), 7.29 – 7.24 (m, 4H), 7.22 – 7.19 (m, 3H), 6.13 – 6.11 (m, 1H), 4.10

– 4.07 (m, 2H), 3.37 – 3.26 (m, 2H), 2.42 – 2.33 (m, 5H), 2.09 – 2.07 (m, 2H), 1.98 (t, J = 2.5 Hz, 1H), 1.43 – 1.31 (m, 4H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 202.2, 143.7, 135.8, 135.5, 129.5 (2C), 128.5 (2C), 127.6 (2C), 126.7, 126.5 (2C), 105.4, 95.9, 76.7, 73.6, 44.8, 36.6, 32.1, 31.1, 29.7, 22.5, 21.3, 13.7; IR (thin film) 3289, 2958, 2929, 2872, 1949, 1712, 1593, 1491, 1462, 1352, 1160, 1091 1001; HRMS (ES+) $\text{C}_{25}\text{H}_{29}\text{NO}_2\text{S}$ [M^+] Calculated: 407.1919; Found: 407.1888; $[\alpha]_{\text{D}}^{20}$ = – 63.8° (c 0.80, CH_2Cl_2).

(*R*_a)-4-methyl-*N*-(3-(2-phenylvinylidene)heptyl)-*N*-(3-(trimethylsilyl)prop-2-yn-1-yl) benzenesulfonamide (14f)

Following the general procedure for preparation of allene-yne *via* silylation of the terminal alkyne, allene-yne **14e** (81.7 mg, 0.20 mmol) in THF (1.6 mL) was reacted with lithium hexamethyldisilylamide (301 μL , 1M in THF, 0.30 mmol) and trimethylsilylchloride (51 μL , 0.40 mmol). Purification of the crude product using a Biotage normal phase automated purification system (12 g SNAP column, gradient of 0 – 8% EtOAc/hexanes) afforded compound **14f** (76.8 mg, 80%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, J = 8.1 Hz, 2H), 7.33 – 7.26 (m, 4H), 7.23 – 7.21 (m, 3H), 6.17 (t, J = 3.0 Hz, 1H), 4.22 – 4.06 (m, 2H), 3.44 – 3.37 (m, 1H), 3.33 – 3.26 (m, 1H), 2.44 – 2.39 (m, 5H), 2.16 – 2.14 (m, 2H), 1.51 – 1.37 (m, 4H), 0.91 (t, J = 7.1 Hz, 3H), –0.02 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 202.2, 143.2, 135.7, 135.4, 129.4 (2C), 128.5 (2C), 127.7 (2C), 126.6, 126.5 (2C), 105.3, 97.8, 95.9, 90.9, 44.6, 37.4, 32.1, 31.1, 29.7, 22.4, 21.5, 13.9, –0.5 (3C); IR (thin film) 3031, 2958, 2929, 2868, 2118, 1953, 1598, 1503, 1458, 1356, 1246, 1164, 1103, 1021, 919; HRMS (ES+) $\text{C}_{28}\text{H}_{37}\text{NO}_2\text{SSi}$ [M^+] Calculated: 479.2314; Found: 479.2278; $[\alpha]_{\text{D}}^{20}$ = – 58.8° (c 1.70, CH_2Cl_2).

(*S*)-5-Butyl-6-phenyl-2-tosyl-8-(trimethylsilyl)-1,2,3,4-tetrahydrocyclopenta [c]azepin-7(6*H*)-one (42f)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **14f** (32.8 mg, 0.068 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (2.7 mg, 0.068 mmol) were reacted in toluene (2.2 mL) for 30 min. Purification of the crude product using a Biotage normal phase automated purification system (4 g SNAP column, gradient of 5 – 25% EtOAc/hexanes) afforded compound **42f** (26.9 mg, 78%) as a white foam. ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.20 – 7.18 (m, 3H), 6.92 – 6.89 (m, 2H), 4.80 (d, J = 16.9 Hz, 1H), 4.53 (d, J = 16.9 Hz, 1H), 3.76 (s, 1H), 3.59 – 3.57 (m, 2H), 2.59 – 2.50 (m, 2H), 2.43 (s, 3H), 1.84 – 1.80 (m, 2H), 1.02 – 0.90 (m, 4H), 0.66 (t, J = 7.1 Hz, 3H), 0.31 (s, 9H); ^{13}C NMR (175 MHz, CDCl_3) δ 207.8, 175.4, 143.5, 140.5 (2C), 139.4, 138.3, 136.0, 129.7 (2C), 128.7 (2C), 127.4 (2C), 127.2 (2C), 126.6, 56.6, 47.3, 46.1, 37.4, 31.5, 29.2, 22.6, 21.6, 13.7, –0.4 (3C); IR (thin film) 3024, 2954, 2921, 2864, 1683, 1593, 1540, 1491, 1454, 1348, 1242, 1164, 1099; HRMS (ES+) $\text{C}_{29}\text{H}_{37}\text{NO}_3\text{SSi}$ [M^+] Calculated: 507.2263; Found: 507.2297; $[\alpha]_{\text{D}}^{20}$ = +105° (c 1.15, CH_2Cl_2).

(*R*_a)-3-(2-Phenylvinylidene)heptyl methanesulfonate (33)

To a stirred solution of alcohol (***R*_a**-**29**) (197.2 mg, 0.911 mmol) in THF (19 mL), cooled to 0 °C (ice bath), was added triethylamine (152 μL , 1.09 mmol) followed by methanesulfonyl chloride (85 μL , 1.09 mmol). The resulting solution was stirred at rt for 18 h. The mixture was diluted with Et_2O (60 mL) and washed with water (2 $\times$ 10 mL). The organic phase was dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification of the crude residue by silica gel chromatography using 40% Et_2O /hexanes afforded compound **33** (247 mg, 92%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.37 – 7.32 (m, 4H), 7.26 – 7.25 (m, 1H), 6.29 – 6.28 (m, 1H), 4.43 – 4.36 (m, 2H), 2.90 (s, 3H), 2.61 – 2.59 (m, 2H), 2.19 –

2.18 (m, 2H), 1.55 – 1.53 (m, 2H), 1.45 – 1.41 (m, 2H), 0.96 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 201.7, 134.7, 128.4 (2C), 126.6, 126.3 (2C), 103.9, 96.6, 67.6, 36.7, 32.3, 31.8, 29.3, 22.1, 13.6; IR (thin film) 3027, 2958, 2925, 2864, 1953, 1597, 1495, 1462, 1364, 1181, 960, 899; HRMS (ES+) $\text{C}_{16}\text{H}_{22}\text{O}_3\text{S}$ [M^+] Calculated: 294.1290; Found: 294.1284; $[\alpha]_{\text{D}}^{20} = -16.3^\circ$ (c 0.95, CH_2Cl_2).

(*R*_a)-Diethyl 2-(3-phenylprop-2-yn-1-yl)-2-(3-(2-phenylvinylidene)heptyl) malonate (16d)

Following the General Procedure for Preparation of Allene-yne *via* alkylation of the malonate moiety, diethyl malonate **34d** (87.2 mg, 0.32 mmol) was reacted with sodium hydride (10.6 mg, 60 wt% in oil, 0.26 mmol), mesylate **33** (62.5 mg, 0.18 mmol) and potassium iodide (44 mg, 0.27 mmol) in DMF-THF (1 : 1, 3.6 mL). Purification of the crude residue by silica gel chromatography using 5% Et_2O /hexanes afforded compound **16d** (58.7 mg, 70%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.31 – 7.27 (m, 5H), 7.25 – 7.14 (m, 5H), 6.17 (t, $J = 2.9$ Hz, 1H), 4.23 (q, $J = 7.2$ Hz, 4H), 3.08 (s, 2H), 2.37 – 2.31 (m, 2H), 2.16 – 2.06 (m, 4H), 1.50 – 1.38 (m, 2H), 1.36 – 1.31 (m, 2H), 1.26 (t, $J = 7.1$ Hz, 6H), 0.87 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 202.0, 170.2 (2C), 135.8, 131.6 (2C), 128.4 (2C), 128.1 (2C), 127.8, 126.4 (2C), 126.3, 123.2, 107.8, 96.0, 84.2, 83.5, 61.6 (2C), 56.9, 32.4, 30.5, 29.8, 27.5, 23.9, 22.5, 14.1 (2C), 13.9; IR (thin film) 2966, 2925, 2864, 1736, 1499, 1462, 1438, 1266, 1189, 1099, 1074, 1025; HRMS (ES+) $\text{C}_{31}\text{H}_{31}\text{O}_4$ [$\text{M}+\text{H}^+$] Calculated: 473.2692; Found: 473.2734; $[\alpha]_{\text{D}}^{20} = -35.7^\circ$ (c 1.85, CH_2Cl_2).

(*S*)-Diethyl 8-butyl-2-oxo-1,3-diphenyl-1,2,6,7-tetrahydroazulene-5,5(4*H*)-dicarboxylate (44d)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **16d** (36.8 mg, 0.078 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (3 mg, 0.0078 mmol) were reacted in toluene (2.6 mL) for 2 h. Purification of the crude residue by flash chromatography (40% Et_2O /hexanes) afforded the title compound **44d** (35.6 mg, 92%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.37 – 7.34 (m, 2H), 7.30 – 7.28 (m, 3H), 7.21 – 7.19 (m, 5H), 4.15 – 4.10 (m, 2H), 4.09 (s, 1H), 4.02 – 3.99 (m, 1H), 3.96 – 3.93 (m, 1H), 3.59 (d, $J = 14.9$ Hz, 1H), 3.50 (d, $J = 14.9$ Hz, 1H), 2.58 – 2.42 (m, 4H), 1.97 – 1.93 (m, 2H), 1.28 – 1.25 (m, 2H), 1.10 – 1.08 (td, $J = 7.1, 2.1$ Hz, 6H), 1.01 – 0.96 (m, 2H), 0.71 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 202.2, 171.3, 171.2, 164.4, 146.3, 140.9, 138.3, 137.1, 131.4, 129.4 (2C), 128.7 (2C), 128.1 (2C), 127.8, 127.6 (2C), 126.8, 61.8, 61.7, 56.1, 55.7, 37.5, 33.5, 32.7, 29.1, 28.6, 22.7, 13.8 (3C); IR (thin film) 2962, 2925, 2856, 1728, 1699, 1605, 1577, 1503, 1454, 1373, 1274, 1234, 1181; HRMS (ES+) $\text{C}_{32}\text{H}_{37}\text{O}_5$ [$\text{M}+\text{H}^+$] Calculated: 501.2641; Found: 501.2623; $[\alpha]_{\text{D}}^{20} = +105^\circ$ (c 1.60, CH_2Cl_2).

(*R*_a)-Diethyl 2-(3-(2-phenylvinylidene)heptyl)-2-(prop-2-yn-1-yl)malonate (16e)

Following the General Procedure for Preparation of Allene-yne *via* alkylation of the malonate moiety, diethyl malonate **34e** (98 mg, 0.49 mmol) was reacted with sodium hydride (16.5 mg, 60 wt% in oil, 0.41 mmol), mesylate **33** (97 mg, 0.27 mmol) and potassium iodide (68.3 mg, 0.41 mmol) in DMF-THF (1 : 1, 5.6 mL). Purification of the crude residue using a Biotage normal phase automated purification system (25 g SNAP column, gradient of 0 – 5% EtOAc /hexanes) afforded compound **16e** (45.5 mg, 42%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.28 – 7.26 (m, 4H), 7.17 – 7.15 (m, 1H), 6.15 (t, $J = 3.0$ Hz, 1H), 4.21 – 4.18 (q, $J = 7.1$ Hz, 4H), 2.84 (d, $J = 2.7$ Hz, 2H), 2.27 – 2.24 (m, 2H), 2.10 – 2.08 (m, 2H), 2.04 – 1.99 (m, 1H), 1.97 (t, $J = 2.7$ Hz, 1H), 1.45 – 1.42 (m, 2H), 1.36 – 1.32 (m, 2H), 1.23 (td, $J = 7.1, 2.8$ Hz, 6H), 0.87 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 201.9, 169.9 (2C), 135.8, 128.4 (2C), 126.5 (2C), 126.4, 107.9, 95.9, 78.8, 71.1, 61.6 (2C), 56.4, 32.4, 30.2, 29.8, 27.2, 22.7, 22.5, 13.8 (2C), 13.7; IR (thin film) 3297,

2962, 2925, 2868, 1740, 1467, 1438, 1270, 1193, 1099, 1070; HRMS (ES+) $C_{25}H_{32}O_4$ [M + H⁺] Calculated: 397.2379; Found: 397.2376; $[\alpha]_D^{20} = -52.7^\circ$ (c 1.5, CH₂Cl₂).

(R_a)-diethyl 2-(3-(2-phenylvinylidene)heptyl)-2-(3-(trimethylsilyl)prop-2-yn-1-yl)malonate (16f)

Following the general procedure for preparation of allene-yne *via* silylation of the terminal alkyne, allene-yne **16e** (44.1 mg, 0.11 mmol) in THF (1 mL) was reacted with lithium hexamethyldisilylamide (200 μ L, 1M in THF, 0.20 mmol) and trimethylsilylchloride (35 μ L, 0.28 mmol). Purification of the crude product using a Biotage normal phase automated purification system (4 g SNAP column, gradient of 1 – 3% EtOAc/hexanes) to afford compound **16f** (43 mg, 84%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.28 – 7.26 (m, 4H), 7.18 – 7.14 (m, 1H), 6.16 – 6.14 (m, 1H), 4.22 – 4.15 (m, 4H), 2.85 (s, 2H), 2.27 – 2.21 (m, 2H), 2.12 – 1.99 (m, 4H), 1.46 – 1.33 (m, 4H), 1.23 (td, *J* = 7.1, 1.8 Hz, 6H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.08 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 202.1, 170.1 (2C), 135.8, 128.5 (2C), 126.5 (2C), 126.4, 107.8, 101.2, 95.9, 88.1, 61.5 (2C), 56.8, 32.3, 30.4, 29.8, 27.5, 24.2, 22.5, 14.0 (2C), 13.9, –0.1 (3C); IR (thin film) 2950, 2921, 2856, 2178, 1941, 1728, 1458, 1437, 1266, 1193, 1030; HRMS (ES+) $C_{28}H_{41}O_4Si$ [M + H⁺] Calculated: 469.2774; Found: 469.2762; $[\alpha]_D^{20} = -34.7^\circ$ (c 2.65, CH₂Cl₂).

(S)-Diethyl 8-butyl-2-oxo-1-phenyl-3-(trimethylsilyl)-1,2,6,7-tetrahydroazulene-5,5(4H)-dicarboxylate (44f)

Following the General Procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **16f** (26.1 mg, 0.056 mmol) and [Rh(CO)₂Cl]₂ (2.2 mg, 0.0056 mmol) were reacted in toluene (1.9 mL) for 2 h. Purification of the crude residue by flash chromatography (15% Et₂O/hexanes) afforded compound **44f** (24.8 mg, 90%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 7.29 – 7.21 (m, 2H), 7.20 – 7.18 (m, 1H), 7.12 – 7.10 (m, 2H), 4.31 – 4.18 (m, 4H), 3.93 (s, 1H), 3.56 (d, *J* = 14.8 Hz, 1H), 3.46 (d, *J* = 14.8 Hz, 1H), 2.56 – 2.54 (m, 1H), 2.50 – 2.46 (m, 1H), 2.42 – 2.39 (m, 2H), 1.94 – 1.87 (m, 2H), 1.29 (td, *J* = 7.1, 2.4 Hz, 6H), 1.26 – 1.22 (m, 1H), 1.11 – 0.94 (m, 3H), 0.71 (t, *J* = 7.3 Hz, 3H), 0.25 (s, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 208.5, 176.3, 171.4, 171.3, 145.6, 141.4, 139.9, 138.9, 128.6 (2C), 127.5 (2C), 126.5, 61.8, 61.7, 57.1, 56.3, 37.8, 34.7, 33.6, 29.1, 28.9, 22.7, 14.0, 14.0, 13.8, –0.3 (3C); IR (thin film) 2954, 2921, 2856, 1732, 1683, 1540, 1454, 1266, 1242, 1185, 1050; HRMS (ES+) $C_{29}H_{41}O_5Si$ [M + H⁺] Calculated: 497.2723; Found: 497.2733; $[\alpha]_D^{20} = +55.6^\circ$ (c 2.1, CH₂Cl₂).

(R_a)-Diethyl 2-(but-2-yn-1-yl)-2-(3-(2-phenylvinylidene)heptyl)malonate (16c)

Following the General Procedure for Preparation of Allene-yne *via* alkylation of the malonate moiety, diethyl malonate **34c** (96 mg, 0.35 mmol) was reacted with sodium hydride (11.7 mg, 60 wt% in oil, 0.29 mmol), mesylate **33** (68.7 mg, 0.19 mmol) and potassium iodide (48.3 mg, 0.29 mmol) in DMF-THF (1 : 1, 4 mL). Purification of the crude residue by flash chromatography (5% Et₂O/hexanes) afforded compound **16c** (60.1 mg, 75%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.26 – 7.24 (m, 4H), 7.16 – 7.13 (m, 1H), 6.14 (t, *J* = 2.8 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 4H), 2.76 – 2.75 (m, 2H), 2.24 – 2.19 (m, 2H), 2.10 – 2.07 (m, 2H), 2.06 – 1.97 (m, 2H), 1.66 (t, *J* = 2.6 Hz, 3H), 1.44 – 1.42 (m, 2H), 1.36 – 1.32 (m, 2H), 1.21 (td, *J* = 7.1, 1.0 Hz, 6H), 0.86 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 202.1, 170.5 (2C), 135.9, 128.4 (2C), 126.5 (2C), 126.4, 107.9, 95.9, 78.8, 73.2, 61.4 (2C), 56.8, 32.4, 30.2, 29.8, 27.3, 23.1, 22.5, 14.0 (2C), 13.9, 3.4; IR (thin film) 2958, 2933, 2860, 1728, 1462, 1446, 1266, 1193, 1103, 1066; HRMS (ES+) $C_{26}H_{35}O_4$ [M + H⁺] Calculated: 411.2535; Found: 411.2528; $[\alpha]_D^{20} = -53^\circ$ (c 1.35, CH₂Cl₂).

(S)-Diethyl 8-butyl-3-methyl-2-oxo-1-phenyl-1,2,6,7-tetrahydroazulene-5,5(4H)-dicarboxylate (44c)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **16c** (33.2 mg, 0.081 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (3.2 mg, 0.0081 mmol) were reacted in toluene (2.7 mL) for 2.5 h. Purification of the crude residue by flash chromatography (30% Et_2O /hexanes) afforded compound **44c** (31.2 mg, 88%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.29 – 7.27 (m, 3H), 7.22 – 7.19 (m, 1H), 7.13 – 7.12 (m, 2H), 4.26 – 4.23 (m, 4H), 3.95 (s, 1H), 3.39 (m, 2H), 2.50 – 2.47 (m, 3H), 2.39 – 2.36 (m, 1H), 1.90 – 1.89 (m, 2H), 1.85 (s, 3H), 1.30 (td, $J = 7.1, 2.5$ Hz, 6H), 1.26 – 1.22 (m, 2H), 1.10 – 0.87 (m, 2H), 0.72 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 204.3, 171.5, 171.4, 164.1, 143.4, 138.5, 137.7, 137.3, 128.6 (2C), 127.5 (2C), 126.6, 61.8 (2C), 55.9, 55.1, 37.1, 33.8, 32.6, 29.1, 28.6, 22.6, 14.0 (2C), 13.8, 8.5; IR (thin film) 2950, 2921, 2856, 1732, 1691, 1597, 1450, 1381, 1361, 1270, 1230, 1185; HRMS (ES+) $\text{C}_{27}\text{H}_{35}\text{O}_5$ $[\text{M}+\text{H}^+]$

Calculated: 439.2484; Found: 439.2467; $[\alpha]_{\text{D}}^{20} = +128^\circ$ (c 2.0, CH_2Cl_2).

(R_a)-(3-(2-((3-Phenylprop-2-yn-1-yl)oxy)ethyl)hepta-1,2-dien-1-yl)benzene (15d)

Following the general procedure for preparation of allene-yne *via* Williamson etherification, alcohol (**R_a**)-**29** (95.8 mg, 0.44 mmol) in THF (1 mL) was reacted with sodium hydride (35.4 mg, 60% dispersion in mineral oil, 0.89 mmol) and (3-bromoprop-1-yn-1-yl)benzene (130 mg, 0.66 mmol) for 11 h. Purification of the crude residue by flash chromatography (1% Et_2O /hexanes) afforded compound **15d** (51.3 mg, 35%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.39 – 7.38 (m, 2H), 7.29 – 7.26 (m, 7H), 7.17 – 7.15 (m, 1H), 6.17 – 6.16 (m, 1H), 4.35 – 4.29 (m, 2H), 3.76 – 3.70 (m, 2H), 2.44 – 2.42 (m, 2H), 2.13 – 2.12 (m, 2H), 1.50 – 1.44 (m, 2H), 1.39 – 1.34 (m, 2H), 0.88 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 202.3, 135.8, 131.7 (2C), 128.5 (2C), 128.3, 128.2 (2C), 126.5 (2C), 126.4, 122.7, 105.5, 95.9, 86.1, 85.2, 68.3, 58.8, 32.8, 32.7, 29.8, 22.5, 13.9; IR (thin film) 3060, 3019, 2962, 2929, 2864, 1949, 1675, 1605, 1495, 1462, 1442, 1352, 1099, 1030; HRMS (ES+) $\text{C}_{24}\text{H}_{27}\text{O}_1$ $[\text{M}+\text{H}^+]$ Calculated: 331.2062; Found: 331.2025; $[\alpha]_{\text{D}}^{20} = -12.4^\circ$ (c 1.05, CH_2Cl_2).

(S)-5-Butyl-6,8-diphenyl-3,4-dihydro-1H-cyclopenta[c]oxepin-7(6H)-one (43d)

Following the General Procedure for the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ Catalyzed Cyclocarbonylation Reaction, allene-yne **15d** (41 mg, 0.124 mmol) and $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (4.8 mg, 0.0124 mmol) were reacted in toluene (4.1 mL) for 30 min. Purification of the crude residue by flash chromatography (30% Et_2O /hexanes) afforded compound **43d** (30.6 mg, 69%) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 7.38 – 7.28 (m, 7H), 7.25 – 7.22 (m, 3H), 4.88 (s, 2H), 4.20 (s, 1H), 4.08 – 4.04 (m, 2H), 2.84 – 2.75 (m, 1H), 2.63 – 2.56 (m, 1H), 2.06 – 1.99 (m, 2H), 1.30 – 1.26 (m, 2H), 1.13 – 1.06 (m, 3H), 0.73 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 201.8, 167.6, 141.8, 138.3, 138.2, 136.1, 130.9, 129.4 (2C), 128.7 (2C), 128.2 (2C), 128.1, 127.6 (2C), 126.9, 70.0, 67.3, 56.2, 36.9, 35.1, 29.7, 22.7, 13.8; IR (thin film) 3064, 3031, 2958, 2925, 2860, 2030, 1695, 1605, 1499, 1458, 1373, 1275, 1140; HRMS (ES+) $\text{C}_{25}\text{H}_{27}\text{O}_2$ $[\text{M}+\text{H}^+]$ Calculated: 359.2011; Found: 359.1980; $[\alpha]_{\text{D}}^{20} = 124.2^\circ$ (c 1.2, CH_2Cl_2).

(R_a)-(3-(2-(But-2-yn-1-yloxy)ethyl)hepta-1,2-dien-1-yl)benzene (15c)

Following the general procedure for preparation of allene-yne *via* Williamson etherification, alcohol (**R_a**)-**29** (105 mg, 0.442 mmol) in THF (1.1 mL) was reacted with sodium hydride (38.8 mg, 60% dispersion in mineral oil, 0.97 mmol) and 1-bromobut-2-yne (97 mg, 0.73 mmol) for 11 h. Purification of the crude residue by flash chromatography (1% Et_2O /hexanes) afforded compound **15c** (33 mg, 27%) as a colorless oil. ^1H NMR (300 MHz,

CDCl₃) δ 7.29 – 7.27 (m, 4H), 7.19 – 7.14 (m, 1H), 6.16 – 6.12 (m, 1H), 4.04 – 4.03 (m, 2H), 3.65 – 3.58 (m, 2H), 2.40 – 2.35 (m, 2H), 2.10 – 2.07 (m, 2H), 1.80 (t, J = 2.3 Hz, 3H), 1.46 – 1.32 (m, 4H), 0.87 (t, J = 7.2 Hz, 3H); ¹³C NMR (175 MHz, CDCl₃) δ 202.2, 135.8, 128.5 (2C), 126.6 (2C), 126.5, 105.5, 95.8, 82.3, 75.2, 68.2, 58.7, 32.8, 32.6, 29.7, 22.5, 13.9, 3.6; IR (thin film) 2954, 2929, 2852, 1495, 1462, 1356, 1140, 1095; HRMS (ES+) C₁₉H₂₅O [M+H⁺] Calculated: 269.1905; Found: 269.1889; [α]_D²⁰ = – 16.1° (c 2.3, CH₂Cl₂).

(S)-5-butyl-8-methyl-6-phenyl-3,4-dihydro-1H-cyclopenta[c]oxepin-7(6H)-one (43c)

Following the General Procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **15c** (19 mg, 0.0719 mmol) and [Rh(CO)₂Cl]₂ (2.8 mg, 0.00719 mmol) were reacted in toluene (2.5 mL) for 45 min. Purification of the crude residue by flash chromatography (20% Et₂O/hexanes) afforded compound **43c** (10 mg, 46%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.44 – 7.27 (m, 2H), 7.27 – 7.15 (m, 3H), 4.82 – 4.80 (m, 2H), 4.03 – 3.94 (m, 3H), 2.59 (t, J = 5.5 Hz, 2H), 1.98 – 1.89 (m, 2H), 1.74 (s, 3H), 1.18 – 0.97 (m, 4H), 0.70 (t, J = 7.1 Hz, 3H); ¹³C NMR (175 MHz, CDCl₃) δ 203.3, 166.8, 140.4, 138.5, 134.9, 134.8, 128.7 (2C), 127.5 (2C), 126.8, 70.4, 69.6, 55.7, 37.1, 36.8, 29.9, 22.7, 13.8, 8.3; IR (thin film) 2950, 2921, 2852, 1691, 1458, 1270, 1152; HRMS (ES+) C₂₀H₂₅O₂ [M+H⁺] Calculated: 297.1855; Found: 297.1834; [α]_D²⁰ = +191° (c 1.0, CH₂Cl₂).

(R_a)-(3-(2-(Prop-2-yn-1-yloxy)ethyl)hepta-1,2-dien-1-yl)benzene (15e)

Following the general procedure for preparation of allene-yne *via* Williamson etherification, alcohol (**R_a**)-**29** (221.6 mg, 2.05 mmol) in THF (2.4 mL) was reacted with sodium hydride (82 mg, 60% dispersion in mineral oil, 0.97 mmol) and propargyl bromide (229 mg, 1.54 mmol) for 11 h. Purification of the crude residue by flash chromatography (0.7% Et₂O/hexanes) afforded compound **15e** (51.9 mg, 20%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.26 – 7.22 (m, 4H), 7.16 – 7.11 (m, 1H), 6.11 (m, 1H), 4.05 (t, J = 2.0 Hz, 2H), 3.66 – 3.58 (m, 2H), 2.38 – 2.33 (m, 3H), 2.10 – 2.04 (m, 2H), 1.43 – 1.30 (m, 4H), 0.84 (t, J = 7.2 Hz, 3H); ¹³C NMR (175 MHz, CD₂Cl₂) δ 202.2, 135.8, 128.4 (2C), 126.5 (2C), 126.4, 105.5, 95.5, 79.9, 73.8, 68.2, 57.9, 32.6, 32.6, 29.7, 22.5, 13.7; IR (thin film) 3309, 2954, 2921, 2856, 1728, 1663, 1593, 1467, 1360, 1254, 1160, 1103; HRMS (ES+) C₁₈H₂₃O [M+H⁺] Calculated: 255.1749; Found: 255.1756; [α]_D²⁰ = – 14.0° (c 1.0, CH₂Cl₂).

(R_a)-Trimethyl(3-((3-(2-phenylvinylidene)heptyl)oxy)prop-1-yn-1-yl)silane (15f)

Following the general procedure for preparation of allene-yne *via* silylation of the terminal alkyne, allene-yne **15e** (48 mg, 0.19 mmol) in THF (1.7 mL) was reacted with lithium hexamethyldisilylamide (340 μ L, 1M in THF, 0.34 mmol) and trimethylsilylchloride (60 μ L, 0.47 mmol). Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, gradient of 0 – 2% EtOAc/hexanes) to afford compound **15f** (39.9 mg, 65%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 7.30 – 7.28 (m, 4H), 7.20 – 7.18 (m, 1H), 6.17 – 6.16 (m, 1H), 4.12 – 4.11 (m, 2H), 3.70 – 3.62 (m, 2H), 2.43 – 2.40 (m, 2H), 2.14 – 2.12 (m, 2H), 1.50 – 1.46 (m, 2H), 1.40 – 1.34 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H), 0.17 (s, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 202.2, 135.7, 128.5 (2C), 126.5 (2C), 126.4, 105.4, 101.6, 95.7, 91.2, 68.2, 58.9, 32.7, 32.6, 29.7, 22.5, 13.9, –0.2 (3C); IR (thin film) 2954, 2925, 2856, 2169, 1949, 1716, 1597, 1491, 1458, 1356, 1250, 1099; HRMS (ES+) C₂₁H₃₁OSi [M+H⁺] Calculated: 327.2144; Found: 327.2128; [α]_D²⁰ = – 18.8° (c 0.85, CH₂Cl₂).

(S)-5-butyl-6-phenyl-8-(trimethylsilyl)-3,4-dihydro-1H-cyclopenta[c]oxepin-7(6H)-one (43f)

Following the General Procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **15f** (25.1 mg, 0.077 mmol) and [Rh(CO)₂Cl]₂ (3 mg, 0.0077 mmol)

were reacted in toluene (2.5 mL) for 45 min. Purification of the crude residue by flash chromatography (15% Et₂O/hexanes) afforded compound **43f** (24.9 mg, 91%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.29 – 7.25 (m, 2H), 7.21 – 7.14 (m, 3H), 4.94 – 4.82 (m, 2H), 4.02 – 3.97 (m, 3H), 2.72 – 2.65 (m, 1H), 2.60 – 2.52 (m, 1H), 2.00 – 1.91 (m, 2H), 1.27 – 1.26 (m, 1H), 1.08 – 1.03 (m, 3H), 0.71 (t, *J* = 7.1 Hz, 3H), 0.21 (s, 9H); ¹³C NMR (175 MHz, CDCl₃) δ 207.5, 180.1, 141.8, 138.8, 138.4, 138.2, 128.7 (2C), 127.4 (2C), 126.6, 69.8, 69.7, 57.4, 37.3, 36.0, 29.7, 22.7, 13.8, –0.3 (3C); IR (thin film) 2954, 2925, 2964, 1695, 1544, 1446, 1250, 1152, 841; HRMS (ES+) C₂₂H₃₁O₂Si [M+H⁺] Calculated: 355.2093; Found: 355.2114; [α]_D²⁰ = +191.0° (c 2.3, CH₂Cl₂).

(*R_a*)-*N*-(3-Cyclopropylprop-2-yn-1-yl)-4-methyl-*N*-(3-(2-phenylvinylidene) heptyl) benzenesulfonamide (14g)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol (*R_a*)-**29** (37.8 mg, 0.18 mmol) in THF (1.3 mL) was reacted with triphenylphosphine (55 mg, 0.21 mmol), *N*-(3-cyclopropylprop-2-yn-1-yl)-4-methylbenzenesulfonamide **30g** (52.3 mg, 0.21 mmol) and diisopropylazodicarboxylate (42 μL, 0.21 mmol) for 11 h. Purification of the crude residue using a Biotage normal phase automated purification system (12 g SNAP column, gradient of 0 – 6% EtOAc/hexanes) afforded compound **14g** (78.2 mg, 78%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.64 (d, *J* = 7.9 Hz, 6H), 7.29 – 7.24 (m, 4H), 7.21 – 7.16 (m, 3H), 6.12 (s, 1H), 4.07 – 3.96 (m, 2H), 3.36 – 3.29 (m, 1H), 3.25 – 3.18 (m, 1H), 2.37 (s, 3H), 2.36 – 2.34 (m, 2H), 2.15 – 2.06 (m, 2H), 1.45 – 1.41 (m, 2H), 1.36 – 1.30 (m, 2H), 0.91 – 0.90 (m, 1H), 0.86 (t, *J* = 7.2 Hz, 3H), 0.56 – 0.53 (m, 2H), 0.26 – 0.24 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 202.3, 143.1, 135.9, 135.5, 129.3 (2C), 128.5 (2C), 127.7 (2C), 126.6, 126.5 (2C), 105.4, 95.9, 89.3, 67.7, 44.6, 37.0, 32.1, 31.2, 29.7, 22.5, 21.5, 13.9, 7.8 (2C), –0.9; IR (thin film) 3027, 2962, 2940, 2860, 2251, 1945, 1593, 1491, 1458, 1348, 1164, 1099; HRMS (ES+) C₂₈H₃₄NO₂S [M+H⁺] Calculated: 448.2310; Found: 448.2329; [α]_D²⁰ = – 83.6° (c 0.55, CH₂Cl₂).

(*S*)-5-butyl-8-cyclopropyl-6-phenyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[*c*]azepin -7(6*H*)-one (42g)

Following the General Procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **14g** (31 mg, 0.069 mmol) and [Rh(CO)₂Cl]₂ (2.7 mg, 0.0069 mmol) were reacted in toluene (2.2 mL) for 35 min. Purification of the crude residue by silica gel chromatography using 40% Et₂O/hexanes afforded compound **42g** (29.1 mg, 88%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.15 (m, 3H), 6.75 – 6.73 (m, 2H), 4.88 (d, *J* = 16.9 Hz, 1H), 4.61 (d, *J* = 16.9 Hz, 1H), 3.67 – 3.65 (m, 1H), 3.64 (s, 1H), 3.57 – 3.53 (m, 1H), 2.68 – 2.63 (m, 1H), 2.53 – 2.48 (m, 1H), 2.41 (s, 3H), 1.78 – 1.72 (m, 2H), 1.62 – 1.59 (m, 1H), 1.30 – 1.27 (m, 1H), 1.21 – 1.18 (m, 1H), 1.08 – 1.06 (m, 1H), 1.01 – 0.96 (m, 1H), 0.94 – 0.90 (m, 1H), 0.87 – 0.85 (m, 2H), 0.80 – 0.77 (m, 1H), 0.66 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 202.7, 162.1, 143.6, 139.4, 138.4, 137.9, 136.0, 135.7, 129.6 (2C), 128.6 (2C), 127.4 (2C), 127.3 (2C), 126.7, 55.3, 47.9, 43.8, 36.9, 31.2, 29.2, 22.6, 21.6, 13.7, 8.3, 5.9, 5.7; IR (thin film) 2962, 2917, 2860, 1695, 1454, 1344, 1172, 1087, 1021; HRMS (ES+) C₂₉H₃₄NO₃S [M+H⁺] Calculated: 476.2259; Found: 476.2271; [α]_D²⁰ = +72° (c 0.75, CH₂Cl₂).

1-(Dimethyl(phenyl)silyl)hept-2-yn-1-ol (24)

To a solution of hept-2-yn-1-ol **23** (5.48 g, 48.9 mmol) in THF (74 mL) cooled to –78 °C was added *n*-BuLi (33.6 mL, 1.0 M in hexanes, 53.7 mmol) and chlorodimethylphenylsilane (9.17 g, 53.7 mmol). After the addition was complete, the bath was removed and the

reaction mixture was stirred at rt for 20 h. The solution was cooled to -78°C and *tert*-butyllithium (34.5 mL, 1.7 M in hexanes, 58.6 mmol) was added dropwise. The mixture was then stirred at -45°C for 2 h. The solution was cooled to -78°C and quenched slowly with a 10% solution of acetic acid in THF (20 mL). The mixture was diluted with NaHCO_3 (100 mL) and extracted with Et_2O (400 mL). The organic phase was separated and extracted with NaHCO_3 (4×150 mL). The organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification of the crude residue using a Biotage normal phase automated purification system (120 g SNAP column, gradient of 1 – 25% EtOAc /hexanes) afforded compound **24** (6.65 g, 55%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.63 – 7.62 (m, 2H), 7.40 – 7.37 (m, 3H), 4.25 (t, $J = 2.4$ Hz, 1H), 2.25 – 2.23 (m, 2H), 1.49 – 1.45 (m, 2H), 1.40 – 1.37 (m, 2H), 0.94 – 0.93 (m, 1H), 0.90 (t, $J = 7.3$ Hz, 3H), 0.43 (d, $J = 7.0$ Hz, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 135.5, 134.3 (2C), 129.6, 127.8 (2C), 89.0, 79.9, 56.2, 30.9, 21.9, 18.7, 13.6, -5.5 , -5.9 ; IR (thin film) 3440, 2954, 2929, 2860, 1248, 1120, 968; HRMS (ES+) $\text{C}_{15}\text{H}_{23}\text{OSi}$ [$\text{M}+\text{H}^+$] Calculated: 247.1518; Found: 247.1496.

Methyl 3-(2-(dimethyl(phenyl)silyl)vinylidene)heptanoate (51)

A 25 mL round bottom flask was charged with propargyl alcohol **24** (1.01 g, 4.1 mmol), trimethylorthoacetate (3.13 mL, 24.5 mmol) and propionic acid (52 μL , 0.69 mmol). The resulting solution was stirred at 160°C for 12 h using a Dean-Stark apparatus. After cooling to rt, the mixture was concentrated under a 10 mmHg vacuum for 2 h. Purification of the crude residue by silica gel chromatography using 2% Et_2O /hexanes afforded compound **51** (940 mg, 76%) as a colorless oil. ^1H NMR (700 MHz, CDCl_3) δ 7.55 – 7.54 (m, 2H), 7.36 – 7.35 (m, 3H), 5.15 (t, $J = 3.4$ Hz, 1H), 3.66 (s, 3H), 2.96 (qd, $J = 15.1$, 3.0 Hz, 2H), 1.99 – 1.98 (m, 2H), 1.37 – 1.31 (m, 4H), 0.88 (t, $J = 7.0$ Hz, 3H), 0.36 (s, 6H); ^{13}C NMR (150 MHz, CDCl_3) 209.8, 172.0, 138.6, 133.7 (2C), 129.0, 127.7 (2C), 91.5, 82.9, 51.7, 38.2, 31.0, 29.8, 22.4, 13.9, -2.28 , -2.32 ; IR (thin film) 2958, 2921, 2860, 1940, 1744, 1434, 1368, 1168; HRMS (ES+) $\text{C}_{18}\text{H}_{27}\text{O}_2\text{Si}$ [$\text{M}+\text{H}$] Calculated: 303.1780; Found: 303.1755.

3-(2-(Dimethyl(phenyl)silyl)vinylidene)heptan-1-ol (25)

A 25 mL round bottom flask was charged with lithium aluminum hydride (4.1 mL of a 1 M solution in Et_2O , 4.02 mmol) and THF (4 mL). The resulting mixture was cooled to 0°C and a solution of ester **51** (810.5 mg, 2.68 mmol) in THF (4.7 mL) was added dropwise. The solution was stirred for 1 h at rt. The reaction mixture was cooled to 0°C (ice bath), diluted with Et_2O (30 mL) and quenched very slowly with water (2 mL). The phases were separated, the organic phase was washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. Purification of the crude residue by silica gel chromatography using 30% Et_2O /hexanes afforded compound **25** (541 mg, 74%) as a colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 7.56 – 7.54 (m, 2H), 7.38 – 7.36 (m, 3H), 5.15 – 5.14 (m, 1H), 3.67 – 3.65 (m, 2H), 2.19 – 2.17 (m, 3H), 1.94 – 1.92 (m, 2H), 1.38 – 1.34 (m, 4H), 0.90 (m, 3H), 0.37 – 0.36 (m, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 209.0, 138.4, 133.6 (2C), 129.0, 127.7 (2C), 93.8, 82.8, 60.8, 34.9, 31.4, 29.9, 22.4, 13.9, -2.2 , -2.3 ; IR (thin film) 3342, 2962, 2933, 2844, 1945, 1458, 1453, 1381, 1242; HRMS (ES+) $\text{C}_{17}\text{H}_{25}\text{OSi}$ [$\text{M}-\text{H}^+$] Calculated: 273.1675; Found: 273.1653.

N-(but-2-yn-1-yl)-*N*-(3-(2-(dimethyl(phenyl)silyl)vinylidene)heptyl)-4-methylbenzenesulfonamide (40)

Following the general procedure for preparation of allene-yne *via* Mitsunobu reaction, alcohol **25** (54.8 mg, 0.2 mmol) in THF (1.5 mL) was reacted with triphenylphosphine (63 mg, 0.24 mmol), *N*-(but-2-yn-1-yl)-4-methylbenzenesulfonamide³⁰**30c** (54 mg, 0.24 mmol) and NaHCO_3 (48 μL , 0.24 mmol) for 2.5 h. Purification of the crude residue by silica gel

chromatography using 5% Et₂O/hexanes afforded compound **40** (46.7 mg, 49%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 5.0 Hz, 2H), 7.39 – 7.37 (m, 3H), 7.29 (d, *J* = 7.4 Hz, 2H), 5.15 – 5.14 (m, 1H), 4.09 (d, *J* = 2.6 Hz, 2H), 3.24 (t, *J* = 8.0 Hz, 2H), 2.44 (s, 3H), 2.22 – 2.20 (m, 2H), 1.96 – 1.95 (m, 2H), 1.56 (t, *J* = 2.3 Hz, 3H), 1.38 – 1.35 (m, 5H), 0.92 (t, *J* = 7.0 Hz, 3H), 0.37 (s, 6H); ¹³C NMR (150 MHz, CDCl₃) δ 208.9, 143.0, 138.5, 136.0, 133.6 (2C), 129.2 (2C), 129.0, 127.7 (2C), 127.6 (2C), 94.1, 82.9, 81.4, 71.7, 44.9, 37.0, 31.3, 29.8 (2C), 22.4, 21.4, 13.9, 3.2, –2.2, –2.3; IR (thin film) 3395, 3064, 2954, 2860, 2165, 1669, 1593, 1438, 1361, 1254, 1160; HRMS (ES +) C₂₈H₃₆NO₂SSi [M–H⁺] Calculated: 478.2236; Found: 478.2238.

5-Butyl-8-methyl-2-tosyl-1,2,3,4-tetrahydrocyclopenta[c]azepin-7(6H)-one (**41**)

Following the General Procedure for the [Rh(CO)₂Cl]₂ Catalyzed Cyclocarbonylation Reaction, allene-yne **40** (33.5 mg, 0.07 mmol) and [Rh(CO)₂Cl]₂ (2.7 mg, 0.007 mmol) were reacted in toluene (2.3 mL) for 6 h. Purification of the crude residue by silica gel chromatography using 65% Et₂O/hexanes afforded compound **41** (25.1 mg, 96%) as a colorless oil. ¹H NMR (700 MHz, CDCl₃) δ 7.58 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.45 (s, 2H), 3.57 (t, *J* = 14.0 Hz, 2H), 2.70 (s, 2H), 2.54 (t, *J* = 6.0 Hz, 2H), 2.39 (s, 3H), 2.00 (t, *J* = 7.4 Hz, 2H), 1.82 (s, 3H), 1.27 – 1.24 (m, 4H), 0.88 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 203.9, 161.5, 143.5, 138.6, 137.0, 136.1, 131.1, 129.4 (2C), 127.0 (2C), 47.9, 45.4, 39.2, 37.0, 32.6, 30.0, 22.6, 21.5, 14.0, 8.2; IR (thin film) 2954, 2929, 2856, 1703, 1462, 1352, 1160; HRMS (ES+) C₂₁H₂₈NO₃S [M+H⁺] Calculated: 374.1790; Found: 374.1806.

6-Methyl-2-tosyl-2,3,4,5-tetrahydrocyclopenta[c]azepin-7(1H)-one (**48**)

To a solution of cyclocarbonylation product **35e** (30 mg, 0.067 mmol) in CH₂Cl₂ (0.1 mL) were added 4 Å molecular sieves (12 mg, activated by heating at 170 °C under vacuum for 12 h) and (*S*)-1-amino-2-methoxymethylpyrrolidine (SAMP) (14 μl, 0.1 mmol). The resulting mixture was stirred at rt for 15 h. The solution was diluted with Et₂O (3 mL), filtered on a Celite plug, rinsed with Et₂O (10 mL) and concentrated under reduced pressure. Purification of the crude residue using a Biotage normal phase automated purification system (4 g SNAP column, gradient of 50 – 70% Et₂O/hexanes) afforded compound **48** (14 mg, 66%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 6.84 (s, 1H), 3.66 (m, 2H), 3.04 (s, 2H), 2.65 (t, *J* = 6.2 Hz, 2H), 2.43 (s, 3H), 1.91 – 1.86 (m, 2H), 1.73 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 203.9, 163.7, 144.3, 139.5, 135.4, 130.1 (2C), 126.9 (2C), 121.3, 116.1, 49.3, 40.9, 30.1, 24.4, 21.6, 8.5; IR (thin film) 2921, 2860, 1683, 1634, 1589, 1450, 1344, 1303, 1164, 1095; HRMS (ES+) C₁₇H₂₀NO₃S [M+H⁺] Calculated: 318.1164; Found: 318.1162.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
Bioactive and Natural Compounds Containing Cyclopentanes with Stereogenic Centers

14 $R^1 = n\text{Bu}$, $R^2 = \text{Ph}$, $X = \text{NTs}$

15 $R^1 = n\text{Bu}$, $R^2 = \text{Ph}$, $X = \text{O}$

16 $R^1 = n\text{Bu}$, $R^2 = \text{Ph}$, $X = \text{C}(\text{CO}_2\text{Et})_2$

17 $R^1 = \text{H}$, $R^2 = \text{Me}$, $X = \text{NTs}$

18 $R^1 = \text{H}$, $R^2 = \text{Me}$, $X = \text{O}$

19 $R^1 = \text{H}$, $R^2 = \text{Me}$, $X = \text{C}(\text{CO}_2\text{Et})_2$

Figure 2.
Allene-yne Precursors

Scheme 1.
APKR: Transfer of Axial Chirality

Scheme 2.
 Synthesis of Racemic and Nonracemic Allenes

Scheme 3.

Synthesis of Allene-ynes 13, 14 and 17 Containing a Tosylamide Tether

Scheme 4.

Synthesis of Allene-ynes 15 and 18 Containing an Oxygen Tether

Scheme 5.

Synthesis of Allene-ynes 16 and 19 Containing a Malonate Tether

Scheme 6.
Cyclocarbonylation Reaction and Triene Formation

Scheme 7.
Desilylation During the Cyclocarbonylation Reaction

Scheme 8.
Postulated Mechanism for the Erosion of Enantiomeric Excesses of Disubstituted Allenes in the Cyclocarbonylation Reaction

Scheme 9.
Absolute Configuration of Cyclocarbonylation Product 35c

Scheme 10.
Synthesis of Compound 48

Table 1

Optimization of the Cyclocarbonylation Reaction Conditions

Entry	$[\text{Rh}(\text{CO})_2\text{Cl}]_2$ (mol %)	Time (h)	T(°C)	Product and yield (%)	Solvent
1	10	3	90	35c (95); 36c (0)	PhMe
2	5	9	90	35c (75); 36c (9)	PhMe
3	10	7	120	35c (61); 36c (35)	PhMe
4	5	7	120	35c (42); 36c (48)	PhMe
5	1	24	120	35c (29); 36c (26)	PhMe
6 ^a	10	24	40	35c ^b (72); 36c (0)	DCE

^aPPh₃ (30 mol %), AgBF₄ (22 mol %);^bYield based on recovered starting material (conversion : 54%)

Table 2

Transfer of Chirality using Trisubstituted Silylated Allene-ynes

Entry	Allene-yne	R	Time (h)	Product, % yield	% ee ^a
1	13a		2.5	35a , 72	>96
2	13b		2.5	35b , 85	>96
3	13c	Me	3	35c , 95	>96
4	13d	Ph	3	35d , 92	>96
5	13e	H	2.5	35e , 66 ^b	>96
6	13f	TMS	3	35f , 89	>99
7	13g		2.3	35g , 83	>99

^aEnantiomeric ratios were determined by HPLC analysis using a ChiralCel OD column;^bCross-conjugated triene was obtained in 13% yield.

Table 3

Transfer of chirality of Trisubstituted Allene-ynes

Entry	Allene-yne ^a	X	R	Time (min)	Product, % yield	% ee ^b
1	14c	NTs	Me	30	42c , 80	74
2	14d	NTs	Ph	30	42d , 75	79
3	14f	NTs	TMS	30	42f , 78	79
4	14g	NTs		30	42g , 88	79
5	15c	O	Me	45	43c , 46	78
6	15d	O	Ph	30	43d , 69	77
7	15f	O	TMS	45	43f , 91	77
8	16c	C(CO ₂ Et) ₂	Me	150	44c , 88	80
9	16d	C(CO ₂ Et) ₂	Ph	120	44d , 92	76
10	16f	C(CO ₂ Et) ₂	TMS	120	44f , 90	76

^aEnantiomeric excess of the disubstituted allenic alcohol >79% ee;^bDetermined by HPLC analysis using a ChiralCel OD column.

Table 4

Transfer of chirality using Disubstituted Allene-ynes

Entry	Allene-yne ^a	X	R	Time (h)	Product, % yield	% ee
1	17c	NTs	Me	4.6	45c , 73	81 ^b
2	17d	NTs	Ph	3	45d , 84	88 ^c
3	17f	NTs	TMS	3	45f , 83	84 ^d
4	18c	O	Me	6.5	46c , 40	45 ^c
5	18d	O	Ph	0.5	46d , 90	52 ^c
6	18e	O	H	1.5	46e , 24	30 ^e
7	18f	O	TMS	7	46f , 76	22 ^d
8	19c	C(CO ₂ Et) ₂	Me	22	47c , 71	58 ^f
9	19d	C(CO ₂ Et) ₂	Ph	1.5	47d , 96	72 ^c
10	19f	C(CO ₂ Et) ₂	TMS	10	47f , 94	50 ^d

^aThe enantiomeric excess of the disubstituted allenic alcohol was >99% ee;^bDetermined using HPLC analysis (ChiralPak IA-3);^cDetermined using HPLC analysis (ChiralCel OD);^dDetermined using SFC analysis (ChiralPak IC);^eDetermined using SFC analysis (ChiralPak IA);^fDetermined using HPLC analysis (Whelk O-1).