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Ring-Closing of 1,7- and 1,8-Enynes of Propargylic *O*,*O*-Acetals by Ruthenium-Catalysed Intramolecular Metathesis

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Acyclic 1,7- and 1,8-enynes with the alkyne moiety directly connected to the asymmetric carbon of an ethyl acetal have been obtained in two steps from the corresponding aldehydes. Ring-closing metathesis of these enynes delivered the corresponding six- and seven-membered cyclic 1,3-dienes in moderate-to-excellent yields. A competitive ethylene insertion into the alkyne moiety leading to trienes was observed for some substrates depending on their structure and relative configuration.

Introduction

Enyne metathesis has emerged as an important method for constructing conjugated dienes,[1,2] which can be transformed into more complex organic molecules.[3] The first enyne metathesis was reported by Katz and Sivavec,[4] who used a tungsten Fischer-type carbene complex. With the advent of Ru–alkylidene catalysts,[5] applications of both intramolecular ring-closing and intermolecular enyne cross-metathesis have rapidly expanded.[2b,2d,2g]

During the course of our synthetic studies on bioactive terpenoids (i.e., salvinorin A,[6] methyl barbascoate[7] or manoalide[8]) we planned to use the *O*,*O*-acetal **1b** as an intermediate (Figure 1).[9]

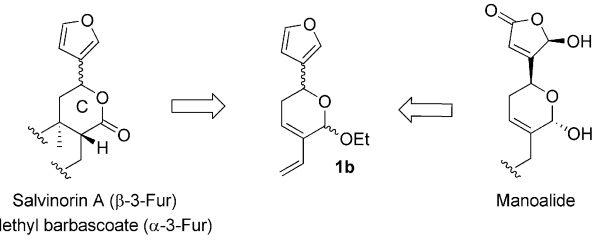


Figure 1. Examples of the possible synthesis of natural products using **1b** as intermediate.

Cyclic *O*,*O*-acetals are rather sensitive and would be well suited to the construction of conjugated dienes by a ring-closing metathesis process. Interestingly, examples of the ring-closing metathesis of linear acetals are scarce in the literature and only two such transformations have been described so far,[10] with allylic *O*,*O*-acetal-tethered enynes giving compounds **2** and **3** (Figure 2) as *cis*/*trans* diastereoisomeric mixtures in moderate yields (36 and 50%, respectively). Dihydropyran and dihydropyridine analogues **4** prepared by *O*- or *N*-tethered ring-closing enyne metathesis (RCEYM) have also been described in the literature (Figure 2).[11]

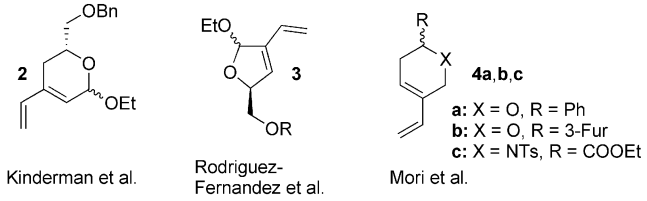
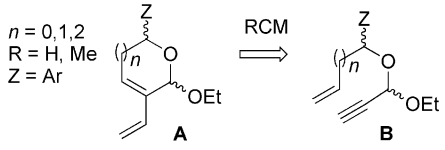


Figure 2. Cyclic compounds prepared by RCEYM of *O*- and *N*-tethered enynes or *O*,*O*-acetal-tethered enynes.

Starting from these few examples, we anticipated that compounds of type **A** could result from the ring-closing metathesis of propargylic *O*,*O*-acetals **B** (Scheme 1). The resulting compounds are highly functionalised and may be useful as precursors for the synthesis of natural products as they possess two double bonds that can be used for further transformations (i.e., cycloadditions) and an alkoxy group adjacent to the ring heteroatom that would give access to the corresponding highly reactive oxocarbenium cation and hence derivatisation at this position.[10,12]



Scheme 1. Allylic *O*,*O*-acetal-tethered ring-closing enyne metathesis.

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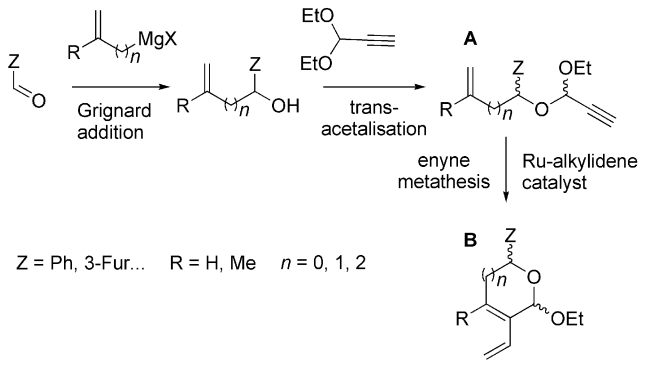
In the work reported herein, we explored the viability of applying this approach to six- and seven-membered rings by describing an efficient synthesis of several unsaturated cyclic *O*,*O*-acetals starting from diastereoisomerically pure *syn* or *anti* enyne precursors. We have also explored for the first time the influence of the relative configuration of the starting *O*,*O*-acetal-tethered enynes on the cyclisation rate and product distribution. Finally, we will discuss herein the possible reaction mechanisms in terms of "yne-then-ene" or "ene-then-yne" pathways to explain the observed products.

Results and Discussion

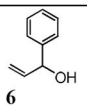
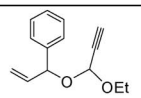
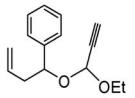
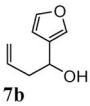
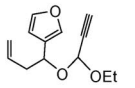
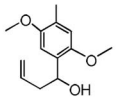
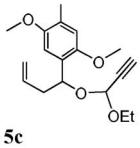
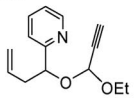
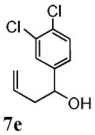
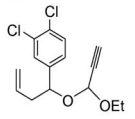
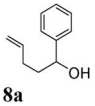
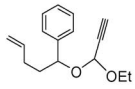
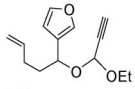
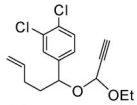
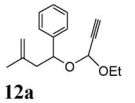
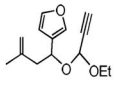
The overall synthesis of 1,3-dienes **A** is outlined in Scheme 2. The ring-closing metathesis precursors were synthesised by transacetalisation of the corresponding alcohols using commercial propiolaldehyde diethyl acetal[13] in the presence of substoichiometric (0.05 equiv.) amounts of camphorsulfonic acid. The secondary alcohols **6**–**9** were prepared by the addition of vinyl-, allyl-, methallyl- and homoallylmagnesium bromide to the corresponding aldehydes (Scheme 2, Table 1).



Scheme 2. Synthesis of 1,3 dienes of type A.

After a few unsuccessful attempts using classic transacetalisation conditions, we found that by mixing the parent alcohols **7a**,**b**,**e**, **8** and **9** with 2 equiv. of propiolaldehyde diethyl acetal in the presence of CSA under vacuum (150 mbar) we obtained the *O*,*O*-acetal-tethered enynes **5a**,**b**,**e**, **11** and **12** in moderate-to-good isolated yields.[9] When we started this study in 2005, there were no reports in the literature about this reaction. Later, Len and coworkers[10b] reported other conditions for the preparation of some *O*,*O*-acetal-tethered enyne precursors of **3** that were less effective with our substrates, delivering the required products in generally lower isolated yields. The solvent-free conditions were not adapted to alcohols **6** and **7c** as these compounds rapidly decompose under acidic conditions. This suggested that when secondary alcohols give rise to a more stabilised carbocation than the oxonium, the reaction would not proceed as the benzylic carbocation undergoes side-reactions more rapidly (entries 1, 4 and 5).[14] Very low conversions of alcohols **6** and **7c** were observed in DMF (0.2 mol L^{-1}) under vacuum and the corresponding acetals **10** and **5c** were isolated in very low yields. In all cases, the products were obtained as *syn*/*anti* diastereoisomeric mixtures.

Table 1. Transacetalisation of secondary alcohols **6**–**9**.

	Alcohol	Solvent	Product	d.r.	Yield
1	 **6**	DMF	 **10**	n.d.	15%[a]
2	 **7a**	–	 **5a**	3/1	78%
3	 **7b**	–	 **5b**	3/1	66%
4	 **7c**	DMF	 **5c**	3/1	24%[a]
5	 **7d**	DMF	 **5d**	1/1	13%[a]
6	 **7e**	–	 **5e**	3/1	65%
7	 **8a**	–	 **11a**	3/1	72%
8	 **8b**	–	 **11b**	3/2	53%
9	 **8e**	–	 **11e**	2/1	66%
10	 **9a**	–	 **12a**	3/1	51%
11	 **9b**	–	 **12b**	3/2	42%

[a] Reaction time more than 1 week, concentration 0.2 mol L^{-1}.

With these precursors in hand, we initially explored the reactivity of enyne **5a**. Whereas in the presence of Grubbs first-generation catalyst G-1 (2 mol-%) in dichloromethane no cyclised compound was observed, even when heated at reflux, the same reaction under ethylene[11] at room temperature led to the expected cyclic acetal **1a** as a 1:3 *cis*/*trans*

mixture after 12 hours in good isolated yield (Figure 3). We could point out a striking difference between the behaviour of enyne acetals such as **5a** and its enyne ether analogue **13**.[11] Regarding the latter, the use of ethylene gas was needed to improve the yield of **4a**, whereas it was mandatory to obtain **1a** (Figure 3). As previously observed in other studies,[15] the use of microwave irradiation reduced the reaction time, but in our case it did not improve the yield of isolated products. Moving to the more active Grubbs G-II and Grubbs–Hoveyda GH-II second-generation catalysts (2 mol-%), the cyclic acetal **1a** was obtained after 20 and 10 min, respectively, under ethylene with microwave irradiation in 86% and 80% isolated yields. Finally, we found that by heating **5a** at reflux in dichloroethane in the presence of 2 mol-% of the G-II catalyst under ethylene for 2 hours, the conversion occurred quantitatively and the cyclic acetal **1a** was obtained in 82% isolated yield. Again, microwave irradiation reduced the reaction time without significant improvement of the isolated yield (86%). The same reaction performed in dichloromethane at room temperature led to a nearly similar isolated yield but required a longer reaction time (overnight).

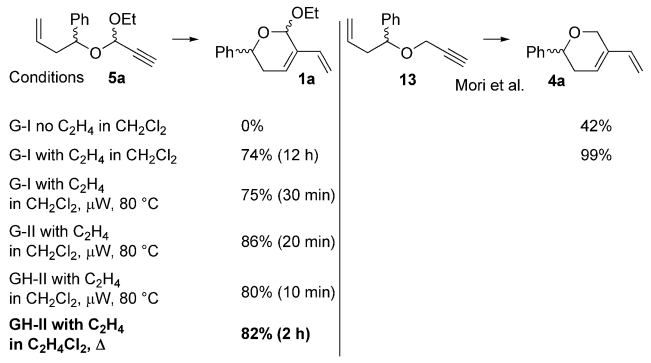


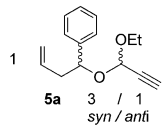
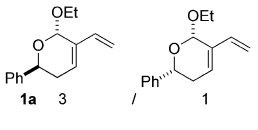
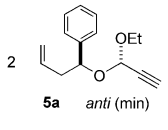
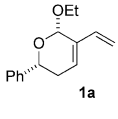
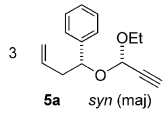
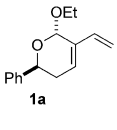
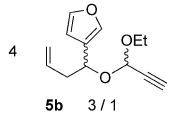
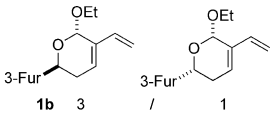
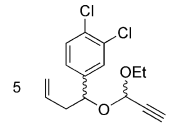
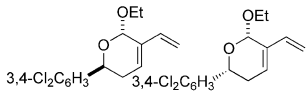
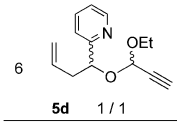
Figure 3. Ring-closing metathesis of enynes **5a** and **13**.

As the diastereoisomeric ratio of the resulting cyclic acetal **1a** appeared to be the same as the ratio of the starting material, the stereospecificity of the metathesis was examined after careful separation of each diastereoisomer of enyne acetal **5a** and cyclic acetal **1a**. When treated under ethylene with 2 mol-% of the G-I or G-II catalyst, each diastereoisomer of **5a** gave quantitatively the corresponding diastereoisomer of **1a** (Table 2, entries 2 and 3). The stereochemical assignment of each diastereoisomer will be developed in the last part of tidine allylic acetal **5d** regardless of the catalyst used (entry 6).

In sharp contrast to allyl enyne acetals **5a**,**b**,**e**, G-I-catalysed ring-closing metathesis reactions of the seven-membered ring precursors **11a**,**b**,**e** as well as of the methallyl acetals **12a**,**b** performed in dichloromethane at room temperature were unsuccessful.

Starting from these initial experiments, we applied the same conditions to other enyne acetals. Good conversions were observed for **5b** and **5e** (Table 2, entries 4 and 5). As

Table 2. Propargylic *O*,*O*-acetal ring-closing metathesis of compounds **5**.

Entry	Substrate	Products	Catalysts[a]	Yield
1	 **5a** 3 / 1 *syn / anti*	 **1a** 3 / 1	G-I G-II	75% 82%
2	 **5a** *anti* (min)	–  **1a**	G-I	80%
3	 **5a** *syn* (maj)	 **1a** –	G-I	82%
4	 **5b** 3 / 1	 **1b** 3 / 1	G-I G-II	73% 81%
5	 **5e** 3 / 1	 **1e** 3 / 1	G-I G-II	75% 80%
6	 **5d** 1 / 1	no reaction	G-I, G-II, GH-2	

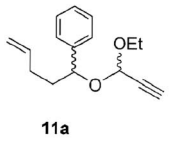
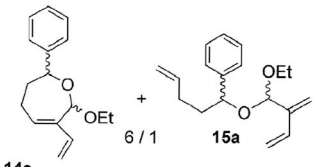
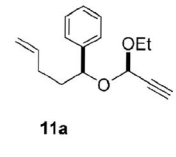
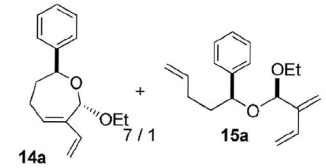
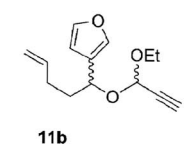
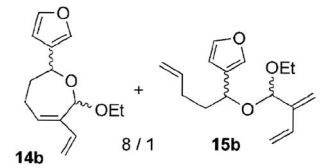
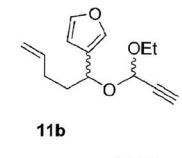
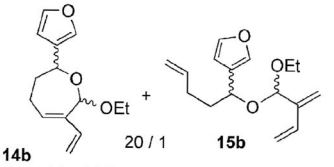
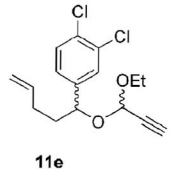
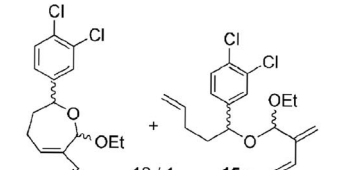
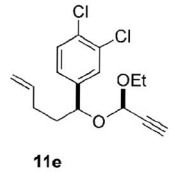
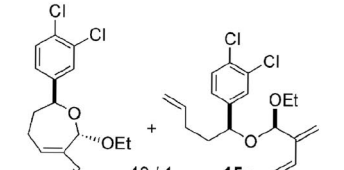
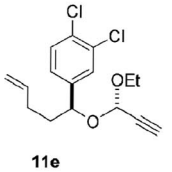
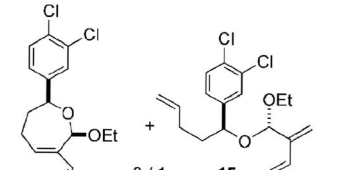
[a] Reactions using G-I (2 mol-%) were performed at room temperature in dichloromethane (12 h), those using G-II (2 mol-%) were performed in dichloroethane (2 h) at reflux, both under ethylene.

previously observed for compound **5a**, the ring-closing enyne metathesis reactions of acetals **5b** and **5e** are stereospecific leading to a 1:3 diastereomeric mixture.

We first focused on the seven-membered ring precursors and selected the G-II catalyst (Table 3). Cycloheptenes **14a**,**b**,**e** were obtained in good isolated yields along with small amounts of the trienes **15a**,**b**,**e** by RCEYM reaction, which did not affect the acetal stereogenic centre (Table 3 entries 2, 4 and 6). Compared with the cyclisation of allyl enyne acetals **5a**,**b**,**e**, larger amounts of catalyst (5%) were required to observe a total conversion in a reasonable time.

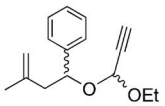
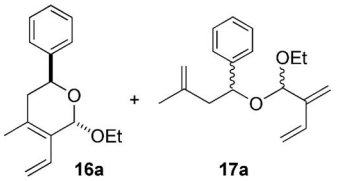
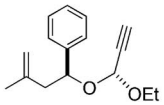
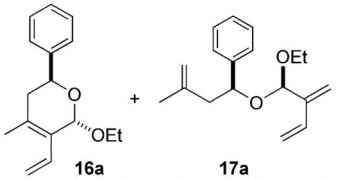
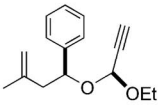
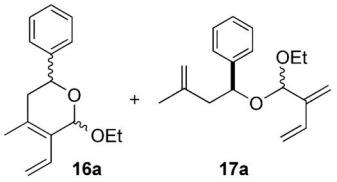
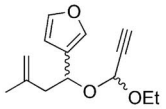
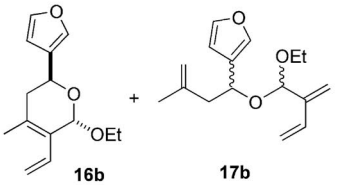
Reactions performed in dichloromethane at room temperature required several days but by heating at reflux in dichloroethane the reaction time decreased to a few hours. In contrast to the enynes **5a**,**b**,**e**, the cyclisation reactions of the major or minor diastereoisomers of enynes **11a**,**b**,**e** occurred at different rates as the reactions of the minor diastereoisomers led to the formation of trienes in larger amounts compared with the major diastereoisomers. In all cases, trienes **15a**,**b**,**e** were formed as an inseparable diastereoisomeric mixture (Table 3, entries 1, 3 and 5) or as

Table 3. Ring-closing enyne metathesis of tethered acetals leading to the corresponding seven-membered rings.

Entry	Substrate Ratio of diastereoisomers of engaged substrate **11**[c]	Products Ratio of **12/13**	Reaction conditions	Yield of **14**
1	 **11a** *syn*:*anti* 1 / 1	 6 / 1 **14a** *trans*/*cis*: 1.5 / 1 **15a** mixture of diastereiosomers	G-II[a] G-II[b]	65% 68%
2	 **11a** *syn*:*anti* 1 / 0	 7 / 1 **14a** *trans*/*cis*: 1 / 0 **15a** one diastereomer	G-II[a] G-II[b]	70% 75%
3	 **11b** *syn*:*anti* 1 / 1	 8 / 1 **14b** *trans*/*cis*: 6 / 4 **15b** mixture of diastereomers	G-II	65%
4	 **11b** *syn*:*anti* 1 / 0	 20 / 1 **14b** *trans*/*cis*: 1 / 0 **15b** one diastereomer	G-II	74%
5	 **11e** *syn*:*anti* 1 / 1	 10 / 1 **14e** *trans*/*cis*: 1.5 / 1 **15e** mixture of diastereomers	G-IIb	82%
6	 **11e** *syn*:*anti* 1 / 0	 10 / 1 **14e** *trans*/*cis*: 1 / 0 **15e** one diastereomer	G-II[b]	78%
7	 **11e** *syn*:*anti* 0 / 1	 3 / 1 **14e** *trans*/*cis*: 0 / 1 **15e** one diastereomer	G-II[b]	48%

[a] Catalyst (5%), ethylene, dichloromethane, 72 h, room temp. [b] Catalyst (5 mol-%), ethylene, dichloroethane, 24 h, reflux. [c] First term of the ratio corresponds to the major *syn* diastereoisomer and the second term to the minor *anti* diastereoisomer of the mixture obtained from the *trans*-ketalisation reaction (Table 1).

Table 4. Ring-closing enyne metathesis of methallyl acetals **12**.

Entry	Substrate Ratio of diastereoisomers of engaged substrate **12**	Products	Reaction conditions	Ratio of **16/17**	Yield of **16**	Yield of **17**
1	 **12a** *anti/syn*: 1 / 3	 **16a** *trans/cis:* 1 / 0 **17a** *anti/syn*: 1 / 1	G-II[a] G-II[b] G-I	1 / 2.6 1 / 2 no conv.	15% 23%	47%
2	 **12a** (maj.) *anti/syn*: 0 / 1	 **16a** *trans/cis*: 1 / 0 **17a** *anti/syn*: 0 / 1	G-II[a] G-III[b]	1 / 2	30%	54%
3	 **12a** (min.) *anti/syn:* 1 / 0	 **16a** **17a** *anti/syn*: 1 / 0	G-II[a] G-III[b]	0 / 1 0 / 1	– –	83%
4	 **12b** *anti/syn*: 1 / 1.5	 **16b** *trans/cis*: 1 / 0 **17b** *anti/syn*: 1 / 1	G-II[a] G-III[b] G-I	1 / 4 1 / 3 no conv.	12%	46%

[a] Determined by GC. [b] Dichloromethane, 36 h, room temperature or dichloroethane, overnight, ethylene, reflux, 5 mol-% catalyst loading.

pure diastereoisomers when the reaction was performed on isolated diastereoisomers of the parent enynes (Table 3, entries 2, 4 and 6).

In no case did the use of the GH-II catalyst instead of the G-II catalyst under ethylene improve the conversion in favour of the cyclised products **14**.

The results obtained with methallyl acetals **12a**,**b** are summarised in Table 4. As previously observed, the reaction had to be performed under ethylene and a loading of 5 mol-% of the G-II catalyst was required for total conversion. Such an observation has already been reported for enynes with different structures of the 1,1-disubstituted alkene fragment.[16] A mixture of only one diastereoisomer of **16a**,**b** and two diastereoisomers of triene **17a**,**b** was observed depending on the catalyst and the conditions used (Table 4, entries 1 and 4). In contrast to allylic and homoallylic enyne acetals **5a**,**b**,**e** and **11a**,**b**,**e**, ring-closing enyne metathesis was less efficient and led to the trienes **17** as the major products when the reaction was performed in dichloromethane at room temperature. In dichloroethane at reflux, the reaction time decreased as well as the yields of trienes **17** in favour of the cyclised products **16**. In this case, the major starting isomer reacted mainly to afford the ethylene insertion product and only 30% of the required cyclised product **16a** was obtained (Table 3, entry 2). The minor isomer delivered quantitatively triene **17a** as only one diastereoisomer in excellent isolated yield (83%) independent of the conditions used (entry 3). Once again, the amount of diene **16** formed was correlated to the diastereoisomeric ratio of the parent enyne acetals.

Determination of the Stereochemistries of Dienes 5, 14 and 16 and Propargylic *O*,*O*-Acetals 1, 11 and 12

Six-Membered-Ring Compounds

Each diastereoisomer of **1a** was cleanly separated by flash chromatography. We chose C_6D_6 as the deuteriated solvent to fully benefit from its known aromatic solvent-induced shift (ASIS). Our previous experiences with simpler *O*,*O*-acetal dienes led us to expect a mixture of conformers in the NMR spectra.[17] However, this was not the case and each diastereoisomer existed as a single conformer on the NMR timescale. A set of ^{1}H irradiation experiments allowed us to clearly assign each proton of each diene and to determine their corresponding coupling constants. The key

features are the benzylic protons (H^2) and their relationship with the allylic protons [H^3 and H^4; see Figure 4]. In both cases, we noted the presence of a large coupling constant ($J > 10$ Hz) along with a small one ($J \approx 3.5$ Hz), which demonstrates a 1,3-*trans*-diaxial relationship between H^2 and one of the methylene protons. Only conformers A and B could account for this 1,3-*trans*-diaxial relationship (Figure 4). These experimental results ruled out, on the NMR timescale, conformers C and D, which have, for both diastereoisomers, the phenyl group in an axial position. In the case of conformer C (*trans*-**1a**), a preliminary examination based upon theoretical data had essentially precluded its existence: this conformer simultaneously suffers from the very unfavourable 1,3-diaxial interaction between phenyl and the H_1 atom and the allylic $A_{1,2}$ strain between the vinyl and ethoxy groups. Having a clear view of the conformational data was unfortunately not enough to determine the *cis*/*trans* stereochemistry. However, taking a closer look at conformers A and B (as well as C and D), we can easily see that only conformer B (i.e., the *cis* diastereoisomer of **1a**) should provide a positive NOE between the acetal proton (H^1) and the benzylic proton (H^2), whereas its *trans* analogue should not. A 2D NOESY experiment confirmed the presence of a positive NOE for only one diene, thus establishing without ambiguity its *cis* stereochemistry (OEt vs. Ph) as well as its conformation (i.e., conformer B vs. D). These results were reinforced by ^{13}C NMR data. For *cis*-**1a**, the chemical shift of the benzylic carbon was 73.6 ppm, whereas its *trans* analogue had, for the same carbon, a chemical shift of 68.4 ppm ($\Delta\delta = -5.2$ ppm relative to *cis*-**1a**). This upfield shift of 5.2 ppm for *trans*-**1a** is consistent with the γ-*syn* effect[18,19] between the ethoxy group and the benzylic carbon (Figure 4). The latter result is also in good agreement with the previously deduced conformation of *trans*-**1a** (i.e., conformer A).

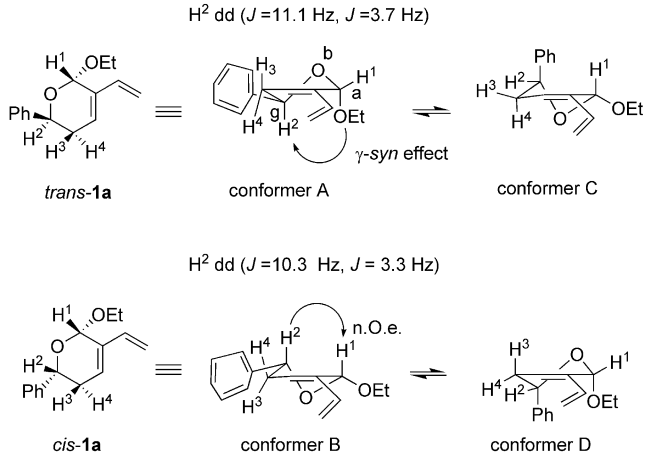


Figure 4. Possible conformers of *trans*- and *cis*-**1a**.

The ^1H and ^{13}C NMR spectra of each stereoisomer of the analogues **1b**,**e** and **12a**,**b** show the same general pattern as observed with **1a**. Thus, based upon the previous results with **1a**, we used the aforementioned γ-*syn* effect in the ^{13}C NMR spectrum to attribute the *cis*/*trans* stereochemistry of each diastereoisomer of the analogues **1a**,**e** and **12a**,**b**.

All the ring-closing metathesis reactions performed on the diastereoisomerically pure starting enyne acetals **1a**, **11a**,**e** and **12a** demonstrated total stereochemical fidelity in the cyclisation reactions and no epimerisation of the acetal stereogenic centre was observed, even after long storage of the starting material on the bench. Consequently, the relative configuration of each enyne acetal **5a** and **16a** as well as by extension **5b** and **16b** can be determined from the relative configurations of the cyclised products (Figure 5).

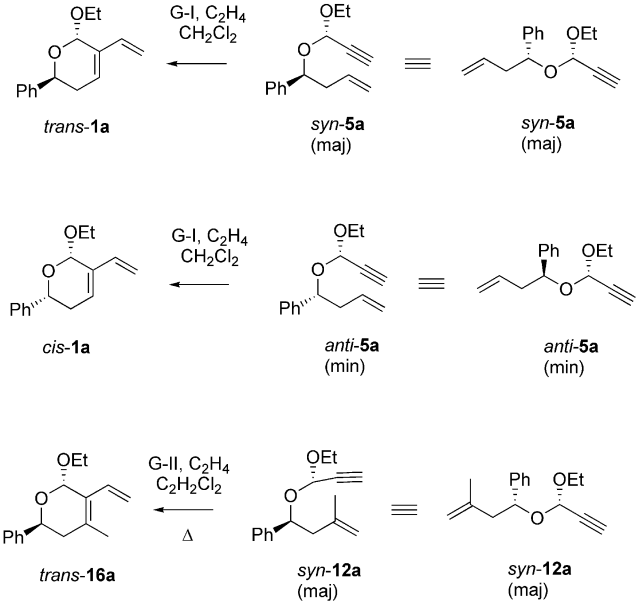


Figure 5. Relative configurations of the starting enynes **5a** and **12a**.

Seven-Membered-Ring Compounds

In the case of seven-membered rings, the situation is more complicated because the cycloheptene ring is believed to exist in stable chair and boat conformers, the latter being of higher energy.[20] However, there has been much disagreement not only about the relative stability of the chair and boat forms, but also about the relative energies of the different transition states during the chair/chair interconversion of cycloheptene, which is highly dependent on the substitution pattern of the seven-membered ring. Nevertheless, despite a proposed equilibrium between the chair and boat conformation in solution at room temperature, the most probable conformation has been experimentally deduced to be the chair.[21] Furthermore, qualitative energy minimisation (MM2) of *cis*- and *trans*-**14a** (Figure 6) showed the chair conformation to be the favoured one for both diastereoisomers.

Starting from the four possible chair-like conformers A–D and by analogy with the six-membered rings **5** and **16**, we assigned the *trans* relative configuration to the major isomer of **14** and the *cis* relative configuration to the minor one. In particular, the presence of a positive NOE for only one diene (the minor one) established without ambiguity its *cis* stereochemistry (OEt vs. Ph) as well as its conformation (i.e., conformer A vs. C). This assignment was confirmed by the γ-*syn* effect in the ^{13}C NMR spectrum (–4 ppm) ob-

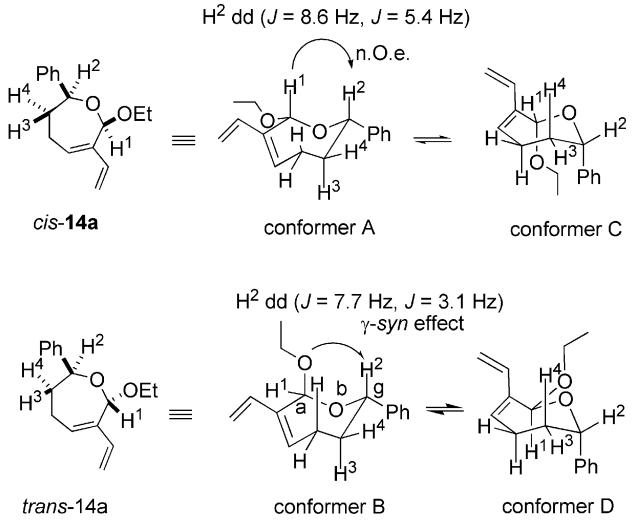


Figure 6. Possible conformers of *trans*- and *cis*-**14a**.

served for the major *trans* diastereoisomer (δ = 70.8 ppm vs. 66.8 ppm).

Finally, from these stereochemical assignments we were able to deduce the *cis* relationship between the aromatic substituent and the ethoxy group of the acetal of the starting enynes **11a**–**e** (Figure 7).

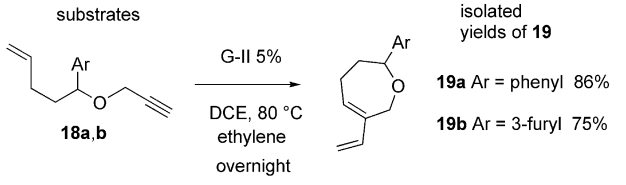


Figure 7. Relative configuration of the starting enyne **11a**.

Discussion

In ring-closing metathesis (RCM) reactions of enynes, the substituents on the multiple bonds are important.[16,22] Steric and electronic factors in the environment of the alkene and alkyne moieties can modify the site of catalyst initiation[22] as well as the rates of cyclisation through enyne metathesis. The presence of geometrically disposed heteroatom groups on the tethering alkyne unit may also interfere through competing bidentate coordination[2b] and recently an accelerating effect of an allylic hydroxy group on ring-closing enyne metathesis has been described.[23]

Two possible reaction pathways have been proposed so far for ruthenium–carbene RCEYM depending on the initial reaction of the ruthenium–carbene complex (=Ru) with the alkynylic or vinylic part of enyne a.[24] In both sequences, two alternative routes can be envisaged (a-*exo* and a-*endo* pathways, Scheme 3).[25]

In either case, the first intermolecular reaction of the enyne substrate with the catalyst has a strong effect on the rate of the second step, which proceeds intramolecularly. Furthermore, the intramolecular step leading to the formation of cyclic intermediates d, e, k and j is controlled by steric interactions between the substituents and stereoelectronic factors such as anomeric effects.

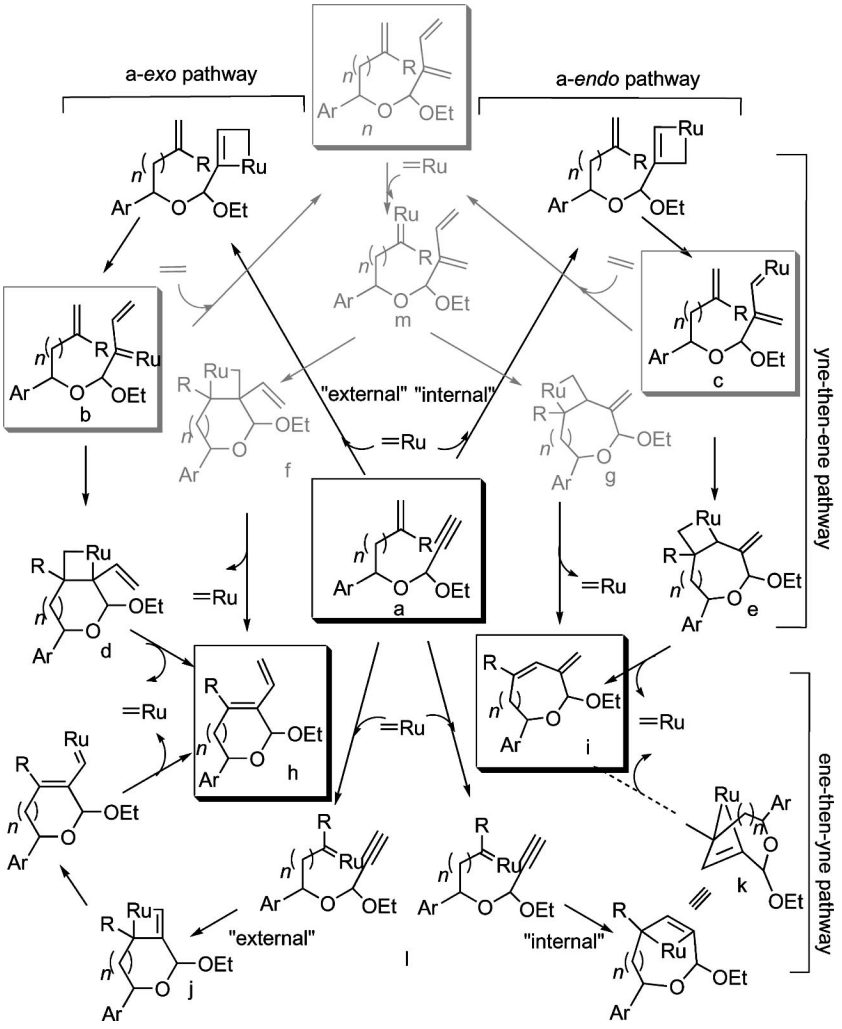
In the case of precursors **5a**,**b**,**e**, which are enynes with a monosubstituted alkene and a terminal alkyne, RCEYM leading to the six-membered ring proceeded smoothly using first- and second-generation ruthenium–carbene complexes under ethylene (Table 2). The products were formed as the same diastereoisomeric mixture of *trans*/*cis* isomers as the starting enynes, which indicates that the reaction does not affect the acetal stereogenic centre and that both precursor diastereoisomers cyclised at a comparable rate. This was confirmed by the cyclisation of isolated diastereoisomers (Table 2, entries 2 and 3). Many kinetic and NMR investigations indicate that in the formation of six- and seven-membered rings, the ene-then-yne pathway yields the smaller *exo* ring isomer.[2g,20,25–27] The ene-then-yne pathway consists of the alkylidenation of the alkene part followed by intramolecular alkyne insertion leading to intermediate j. This pathway is in good agreement with our results and is supported by the observed ethylene effect on the reaction rate using the conditions of Mori et al.[3,11a] In this intermediate, substituent interactions (i.e., diaxial interactions) are less important than in bicyclic intermediate d, which arises from alkyne insertion first, independent of the relative configuration of the parent enynes.

The second-generation ruthenium–carbene complex G-II with 5 mol-% loading was required to form the seven-membered dienes **14a**,**b**,**e** and a higher temperature was necessary to perform the reaction in a reasonable time (Table 3). Both diastereoisomers of the parent enynes **11a**,**b**,**e** gave the cyclised dienes **14a**,**b**,**e** in comparable overall rates with the simultaneous formation of small amounts of trienes **15a**,**b**,**e**, probably by cross-metathesis between ethylene gas and the alkyne part of the starting enyne. However, the cyclisation of each diastereoisomer did not occur at the same rate because the minor diastereoisomer (*anti*) led to a larger amount of triene than the major one (*syn*).

Regarding the cyclisation of methallyl acetal precursors **12** (Table 4), only the major *syn* diastereoisomers of the parent enynes gave the cyclised dienes **14** with the *trans* relative configuration (Ar vs. OEt) in moderate yields with 5 mol-% of the carbene complex G-II. The minor diastereoisomer (*anti* isomer) led selectively to the corresponding trienes **15** by ethylene insertion into the alkyne part of the starting enyne.

The cross-metathesis process leading to triene formation is competitive because the RCEYM reaction, which yields the *exo* ring isomers **14** or **16**, is slower. This has recently been demonstrated by Hansen and Lee[27] for the formation of large ring, which occurs with a relatively low rate of macrocyclisation by enyne metathesis.

In addition to the steric and electronic effects of the substituents, stereoelectronic factors may play an important role in the stability of the bicyclic intermediates through the anomeric effect. To evaluate the influence of the ethoxy

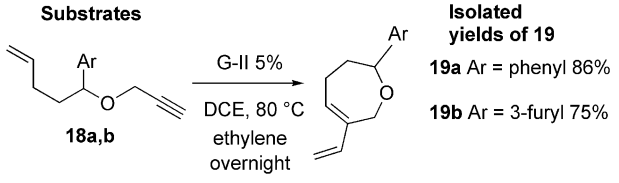


Scheme 3. Yne-then-ene and ene-then-yne pathways for the RCEYM reactions. Routes printed in grey represent triene formation by cross-metathesis with ethylene and subsequent potential reactions.

group on the RCEYM reaction, we prepared the corresponding ethers **18a**,**b** (Scheme 4) and **20a**,**b** (Scheme 5) and submitted them to RCEYM conditions.

Seven-Membered Rings

We prepared enynes **18a**,**b** from the corresponding aldehydes[11b] and conducted the RCEYM reactions in the presence of the G-II catalyst (5 mol-%) and under ethylene (Scheme 4).



Scheme 4. Homoallylic *O*-tethered enyne ring-closing metathesis.

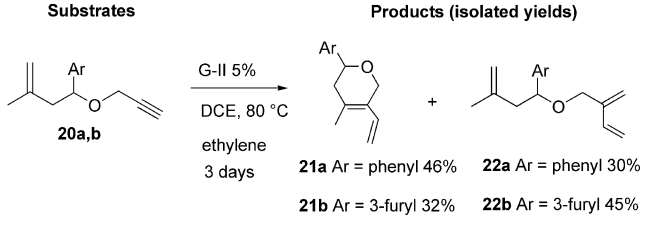
In contrast to the enynes **11a**,**b**,**e**, Ru-catalysed RCM reactions of enynes **18a**,**b** gave **19a**,**b** in 86 and 75% yields, respectively, without any triene formation. We observed that the reaction was also effective but required a longer reaction time when the G-I catalyst (6 mol-%) was used instead of G-II.

These results clearly indicate that removal of the ethoxy group prevented triene formation and led to shorter reaction times. In the case of enynes **11a**,**b**,**e**, the rate of the second intramolecular step leading to intermediates j or d of the minor diastereoisomer decreases due to steric interactions and the formation of intermediate n becomes competitive.

Six-Membered Rings (from Methallyl Precursors)

Enynes **20a**,**b** were prepared and submitted to RCEYM (Scheme 5). The reaction performed with the G-I catalyst did not proceed. The reaction proceeded very slowly (more than 3 days) in the presence of carbene complex G-II

(5 mol-%) in dichloroethane at reflux to give 1,3-dienes **21a**,**b** along with the trienes **22a**,**b**. Under these conditions, about 20% of both substrates **20a**,**b** remained in the reaction mixture after 3 days (Scheme 5). Thus, triene formation occurred with both methallylic *O*-tethered and *O*,*O*-acetal enynes **20a**,**b** and **12a**,**b**, respectively.



Scheme 5. Methallylic *O*-tethered enyne ring-closing metathesis.

Geminal alkene substitution retards the competitive alkylidenation in favour of the intermolecular alkyne insertion by the yne-then-ene pathway. This pathway leads in the case of enynes **12a**,**b** to vinylcarbene intermediate b for which cyclisation to bicyclic intermediate d is subject to several diaxial interactions (Scheme 3): two possible 1,2-diaxial interactions between vinyl and ethoxy and vinyl and methyl (R) substituents, three 1,3-diaxial interactions between ethoxy and methyl (R), ethoxy and aromatic (Ar) substituents and finally methyl (R) and aromatic (Ar) substituents. Moreover, stereoelectronic factors may play an important role in the stability of the bicyclic intermediates through the anomeric effect. On the other hand, initiation at the double bond of methallylic substrates cannot be ruled out. The rate of the intramolecular cyclisation leading to intermediate d may be low due to steric constraints giving back the starting enyne a, which can react through the yne-then-ene pathway. For both intermediates d and j the *trans* isomers are favoured due to the conjugation of the anomeric effect with minimised 1,3-diaxial strains between the substituents. The *cis* isomers are less stable and the reaction proceeds through intermediate n leading to triene formation.

The lower reaction rate observed for **20a**,**b** compared with the corresponding acetals **12a**,**b** is quite surprising but can be explained by a higher reactivity of the alkyne part towards the ruthenium catalyst in substrates **12a**,**b** due to the presence of a second oxygen atom at the α-position. Furthermore, the stabilisation of intermediates d or j through the anomeric effect can accelerate the cyclisation process.

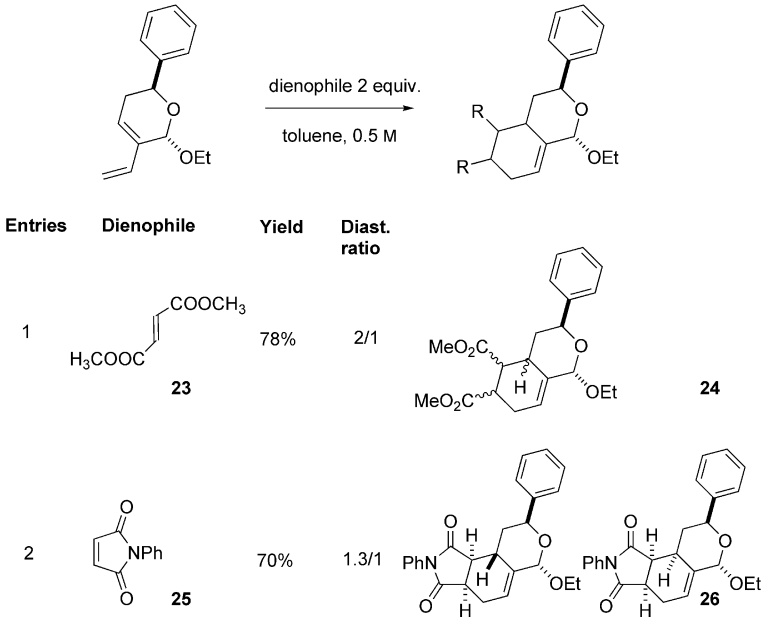
The diverse synthetic utility of *exo* six-membered rings was further demonstrated by the conversion of pure *trans*-**1a** into cycloadducts **24** and **26** by Diels–Alder reaction with dienophiles **23** and **25** in toluene at reflux (Scheme 6). Slight facial selectivity was observed leading to a diastereoisomeric mixture of cycloadducts resulting from preferential bottom-face attack of dienophiles on the 1,3-diene.

Investigation of the possible diastereomeric control with chiral dienophiles[28] aimed at the synthesis of terpenoids (i.e., salvinorin J)[29] will be reported in due course.

Conclusions

We have demonstrated the efficient transformation of allylic and homoallylic *O*,*O*-acetals **5** and **11** into the corresponding six- and seven-membered cyclic 1,3-dienes **1** and **14** by enyne ring-closing metathesis using ruthenium–carbene catalysts. These dienes appeared to be suitable substrates for Diels–Alder cycloaddition as shown by two examples.

Ru-catalysed ring-closing enyne metathesis reactions involving enynes **5** and **11** are compatible with the ene-then-yne mechanism. The rate of cyclisation is governed by the



Scheme 6. Cycloaddition reactions of diene **1a** with dienophiles **23** and **24**.

substitution and stereoelectronic patterns of the parent enynes. In the case of the homoallylic and methallylic substrates **11** and **12**, the formation of the corresponding trienes **13** and **17** was observed in a ratio that is correlated to the relative configuration of the parent enynes. These trienes resulted from ethylene insertion into the alkyne part of the enyne by the competitive yne-then-ene mechanism.

Experimental Section

General: Reagents and solvents were purchased and used without further purification (reagent grade quality). THF was distilled from sodium benzophenone ketyl. Dichloromethane was distilled from CaH_2. Column chromatography: silica gel 60 (230–400 mesh, 0.040–0.063 mm). Demetalled silica gel was prepared according to the published procedure.[11a] Thin-layer chromatography (TLC) was performed on glass sheets coated with silica gel 60 F_{254} (unless otherwise stated) and visualisation by UV light. IR spectra were recorded with a Universal ATR instrument. ^1H and ^{13}C NMR spectra were recorded at 200, 300 or 400 MHz. Chemical shifts are reported as δ values (ppm) with the solvent ($CDCl_3$) resonance as reference (δ = 7.26 ppm). Chemical shift data are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, app. = apparent, mc = multiplet centre, coupling constants *J* [Hz], signal integration. The following known compounds were isolated as pure samples and their characterisation data matched those of the reported compounds: **6**,[11a] **4a**,[30] **7a**–**7e**,[30,31] **8a**–**8e**,[32,33] **9a**–**b**[34] and **13**.[11a] The G-I, G-II and GH-II catalysts were purchased from Aldrich.

Synthesis of Homoallylic, Methallylic and Allylic Alcohols

General Procedure for Methallylic and Allylic Addition (G1): Methallyl- or allylmagnesium bromide (1.2 equiv., 1 M and 0.5 M in diethyl ether purchased by Aldrich) was added to a stirred solution of 0.1 M aldehyde (1 equiv.) in diethyl ether over a 30 min period (5–20 mmol scale). The mixture was stirred for 2 h and poured into an aqueous NH_4Cl solution. The layers were separated and the aqueous phase was extracted with diethyl ether. The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residual oil was bulb-to-bulb distilled to give the corresponding alcohols as colourless liquids.

General Procedure for Homoallylic Addition (G2): The Grignard reagent solution was prepared from magnesium turnings (1.2 equiv.) and 4-bromo-1-butene (1.15 equiv.) in anhydrous diethyl ether at 0 °C under nitrogen and stirred for 1 h (5–20 mmol scale). Aldehyde (1 equiv., 0.5 M in diethyl ether) was added dropwise to the cold (0 °C) stirred solution. The reaction mixture was stirred at room temperature for 1 h and hydrolysed with a saturated ammonium chloride solution. The aqueous phase was extracted with diethyl ether and the combined organic layers were dried and the solvents evaporated to dryness. Distillation afforded the corresponding homoallylic alcohols as yellow or colourless oils.

1-(2,5-Dimethoxy-4-methylphenyl)but-3-en-1-ol (7c): Compound **7c** was prepared following the general experimental procedure G1 starting from 2,5-dimethoxy-4-methylbenzaldehyde. Bulb-to-bulb distillation (107 °C under 20 Torr) gave 1-(2,5-dimethoxy-4-methylphenyl)but-3-en-1-ol as a white solid (81%). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.87 (s, 1 H), 6.70 (1 H), 5.87 (dddd, *J* = 17.1, 10.2, 7.4, 6.6 Hz, 1 H), 5.19–5.10 (m, 2 H), 4.94 (dd, *J* = 7.9, 4.9 Hz, 1 H), 3.81 (s, 6 H), 2.65–2.42 (m, 2 H), 2.22 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.8 (CH), 150.0 (CH), 135.3 (CH), 129.7 (CH), 126.0 (CH), 126.8 (CH), 117.5 (CH), 113.9 (CH), 109.5 (CH), 69.6 (CH), 55.9 (CH_3), 42.2 (CH_2), 16.2 (CH_3) ppm. HRMS (ESI): calcd. for $C_{13}H_{18}Na_1O_3$ $[M + Na]^+$ 245.115; found 245.116.

1-(Pyridin-2-yl)but-3-en-1-ol (7d): Compound **7d** was prepared following the general experimental procedure G1 starting from pyridine-2-carbaldehyde. Bulb-to-bulb distillation (112 °C under 20 mbar) gave 1-(pyridin-2-yl)but-3-en-1-ol as a yellow oil (90%). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.56 (d, *J* = 4.9 Hz, 1 H), 7.71 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.31 (d, *J* = 7.7 Hz, 1 H), 7.22 (dd, *J* = 7.7, 4.9 Hz, 1 H), 5.84 (ddt, *J* = 16.9, 10.5, 7 Hz, 1 H), 5.13 (app. d, *J* = 7.0 Hz), 5.09 (app. t, 1 H), 4.83 (dd, *J* = 7.2, 4.8 Hz, 1 H), 3.66 (br. s, OH), 2.70–2.60 (m, 1 H), 2.50 (ddt, *J* = 14.2, 7.4, 1.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.4 (C), 148.0 (CH), 136.8 (CH), 134.1 (CH), 122.4 (CH), 120.5 (CH), 118.0 (CH_2), 72.2 (CH), 42.9 (CH_2) ppm. HRMS (ESI): calcd. for $C_9H_{11}Na_1O_1$ $[M + Na]^+$ 172.073; found 172.072.

1-(3,4-Dichlorophenyl)but-3-en-1-ol (7e): Compound (**7e**) was prepared following the general experimental procedure G1 starting from 3,4-dichlorobenzaldehyde. Bulb-to-bulb distillation (125 °C under 20 mbar) gave 1-(3,4-dichlorophenyl)but-3-en-1-ol as a yellow oil (93%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 2.1 Hz, 1 H), 7.42 (d, *J* = 8.3 Hz, 1 H), 7.19 (dd, *J* = 8.3, 2.1 Hz, 1 H), 5.78 (dddd, *J* = 18.1, 9.4, 7.7, 6.5 Hz, 1 H), 5.21 (app. s, 1 H), 5.17 (m, 1 H), 4.72 (dd, *J* = 7.8, 4.8 Hz, 1 H), 2.57–2.38 (m, 2 H), 1.97 (br. s, OH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.1 (C), 133.6 (CH), 132.6 (C), 131.4 (C), 130.4 (CH), 127.9 (CH), 125.2 (CH), 119.4 (CH_2), 72.0 (CH), 43.9 (CH_2) ppm.

1-(3,4-Dichlorophenyl)pent-4-en-1-ol (8e): Compound **8e** was prepared following the general experimental procedure G2 starting from 3,4-dichlorobenzaldehyde. Bulb-to-bulb distillation (95 °C under 5 mbar) gave 1-(3,4-dichlorophenyl)pent-4-en-1-ol as a yellow oil (80%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 2.1 Hz, 1 H), 7.41 (d, *J* = 8.3 Hz, 1 H), 7.17 (dd, *J* = 8.3, 2.1 Hz, 1 H), 5.82 (ddt, *J* = 17.1, 10.2, 6.6 Hz, 1 H), 5.05 (ddd, *J* = 17.1, 3.2, 1.6 Hz, 1 H), 5.01 (ddd, *J* = 10.2, 3.2, 1.6 Hz, 1 H), 4.67 (dd, *J* = 7.4, 5.1 Hz, 1 H), 4.65 (br. s, OH), 2.15–2.01 (m, 2 H), 1.90–1.69 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.0 (C), 137.72 (CH), 132.5 (C), 131.2 (C), 130.4 (CH), 128.7 (C), 127.93 (CH), 125.2 (CH), 115.3 (CH_2), 72.7 (CH), 38.1 (CH_2), 29.8 (CH_2) ppm. HRMS (ESI+): calcd. for $C_{11}H_{13}Cl_2O$ $[M + H]^+$ 231.00; found 231.03.

1-(Furan-3-yl)-3-methylbut-3-en-1-ol (9b): Compound **9b** was prepared following the general experimental procedure G1 starting from 3-furaldehyde. Bulb-to-bulb distillation (100 °C under 10 mbar) gave 1-(furan-3-yl)-3-methylbut-3-en-1-ol as a yellow oil (79%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.35 (m, 2 H), 6.4 (app. s, 1 H), 4.89 (app. s, 1 H), 4.82 (app. s, 1 H), 4.78 (td, *J* = 6.9, 1.6 Hz, 1 H), 2.45–2.40 (m, 2 H), 2.30 (br. s, OH), 1.77 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.0 (CH), 141.9 (C), 138.8 (CH), 128.5 (CH), 113.8 (CH_2), 108.4 (CH), 64.2 (CH), 46.5 (CH_2), 22.2 (CH_3) ppm. HRMS (ESI+): calcd. for $C_9H_{12}O_2$ $[M + H]^+$ 152.191; found 152.190.

Synthesis of Enyne *O*,*O*-Acetals

General Procedure for Transacetalisation: Homoallylic, methallylic or allylic alcohol (1 equiv.), 3,3-diethoxypropyne (2.1 equiv.) and camphorsulfonic acid (0.05 equiv.) were mixed at room temperature (5–10 mmol scale). The reaction mixture was stirred at 175 mbar (with an evaporator) for 15 h at 40 °C. The reaction was monitored by TLC. The crude product was diluted with Et_2O, washed with a saturated solution of $NaHCO_3$ and then with brine, dried with $NaSO_4$ and evaporated to dryness. The two diastereoisomers were

separated by flash chromatography on silica gel (toluene/cyclohexane, 10:90) to afford the *anti* (*like*) and *syn* (*unlike*) products as colourless oils.

Compounds **10** and **5c** were prepared in DMF (0.2 M) under vacuum.

Compound 5a: Compound **5a** was prepared following the general procedure (starting from **7a**). Chromatography on silica gel (toluene/cyclohexane, 10:90) gave a 3:1 *anti*/*syn* mixture of **5a** in 78% yield as a colourless oil.

R_f (mixture of diastereoisomers) = 0.4 (cyclohexane/Et_2O, 40:1, UV and vaniline).

1-(1-Ethoxyprop-2-ynyloxy)but-3-enylbenzene [*anti*-5a (*like*)]: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.35–7.22 (m, 5 H), 5.72 (ddt, J = 17.1, 10.2, 7.0 Hz, 1 H), 5.04 (d, J = 1.8 Hz, 1 H), 5.05–5.02 (m, 1 H), 4.98–4.94 (m, 1 H), 4.67 (dd, J = 7.8, 6.0 Hz, 1 H), 3.52 (q, J = 7.1 Hz, 1 H), 2.59 (ddd, J = 14.1, 7.9, 6.9 Hz, 1 H), 2.46 (d, J = 1.8 Hz, 1 H), 2.39 (ddd, J = 14.1, 7.9, 6.9 Hz, 1 H), 1.10 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.4 (C), 128.4 (2 CH), 127.8 (CH), 127.0 (2 CH), 124.4 (CH), 117.0 (CH_2), 94.6 (CH), 78.6 (CH), 76.1 (CH), 73.5 (C), 59.9 (CH_2), 42.5 (CH_2), 15.1 (CH_3) ppm. HRMS (ESI+): calcd. for $C_{15}H_{19}O_2$ [M + H]$^+$ 231.139; found 231.138.

1-(1-Ethoxyprop-2-ynyloxy)but-3-enylbenzene [*syn*-5a (*unlike*)]: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.35–7.22 (m, 5 H), 5.76 (ddt, J = 17.1, 10.2; 7.0 Hz, 1 H), 5.24 (d, J = 1.8 Hz, 1 H), 5.10–5.00 (m, 2 H), 4.69 (t, J = 6.7 Hz, 1 H), 3.74 (dq, J = 9.3, 7.3 Hz, 1 H), 3.40 (dq, J = 9.3, 7.1 Hz, 1 H), 2.72–2.66 (m, 1 H), 2.54–2.44 (m, 1 H), 2.51 (d, J = 1.8 Hz, 1 H), 1.05 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.1 (C), 128.4 (2 CH), 127.8 (CH), 127.0 (2 CH), 124.1 (CH), 117.2 (CH_2), 96.1 (CH), 78.4 (CH), 77.9 (CH), 74.2 (C), 61.7 (CH_2), 42.4 (CH_2), 15.1 (CH_3) ppm. HRMS (ESI+): calcd. for $C_{15}H_{18}NaO_2$ [M + Na]$^+$ 253.120; found 253.116.

Compound 5b: Compound **5b** was prepared following the general procedure (starting from **7b**). Chromatography on silica gel (toluene/cyclohexane, 10:90) gave a 3:1 *anti*/*syn* mixture of **5b** in 66% yield as a colourless oil. R_f (mixture of diastereoisomers) = 0.7 (cyclohexane/Et_2O, 3:1, UV and *p*-anisaldehyde).

3-[1-(1-Ethoxyprop-2-ynyloxy)but-3-enyl]-furan [*anti*-5b (*like*)]: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.39 (m, 1 H), 7.25 (m, 1 H), 6.42 (m, 1 H), 5.77 (m, 1 H), 5.10 (d, J = 1.2 Hz, 1 H), 5.00 (m, 2 H), 4.75 (dd, J = 8.0, 6.0 Hz, 1 H), 3.79 (q, J = 6 Hz, 1 H), 2.70–2.35 (m, 2 H), 2.53 (d, J = 1.2 Hz, 1 H), 1.17 (t, J = 6.0 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.7 (CH), 140.7 (CH), 129.7 (CH), 125.2 (C), 117.0 (CH_2), 91.0 (CH), 88.3 (CH), 78.1 (CH), 70.5 (C), 59.9 (CH_2), 40.8 (CH_2), 15.2 (CH_3) ppm. HRMS (ESI$^+$): calcd. for $C_{13}H_{17}O_3$ [M + H]$^+$ 221.1174; found 221.1178.

3-[1-(1-Ethoxyprop-2-ynyloxy)-but-3-enyl]furan [*syn*-5b (*unlike*)]: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.39 (m, 1 H), 7.25 (m, 1 H), 6.40 (m, 1 H), 5.77 (m, 1 H), 5.15 (d, J = 1.0 Hz, 1 H), 5.00 (m, 2 H), 4.59 (dd, J = 8.0, 6.0 Hz, 1 H), 3.79 (q, J = 6 Hz, 1 H), 2.70–2.35 (m, 2 H), 2.50 (d, J = 1.0 Hz, 1 H), 1.04 (t, J = 6.0 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.7 (CH), 140.7 (CH), 129.7 (CH), 125.2 (C), 117.0 (CH_2), 91.5 (CH), 89.5 (CH), 78.6 (CH), 70.5 (C), 59.9 (CH_2), 40.7 (CH_2), 15.1 (CH_3) ppm.

Compound 5e: Compound **5e** was prepared following the general procedure (starting from **7e**). Chromatography on silica gel (toluene/cyclohexane, 30:70) gave a 3:1 *anti*/*syn* mixture of **5e** in 65% yield as a colourless oil. R_f (mixture of diastereoisomers) = 0.6 (cyclohexane/Et_2O, 30:1, UV and vaniline).

1,2-Dichloro-4-[1-(1-ethoxyprop-2-ynyloxy)but-3-enyl]benzene (5e): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.39 (m, 2 H), 7.19–7.16 (m, 2 H), 5.83–5.61 (m, 1 H), 5.27 (d, J = 1.8 Hz, 0.6 H, one diastereoisomer), 5.21–5.14 (m, 0.6 H, one diastereoisomer), 5.10 (d, J = 1.8 Hz, 0.3 H, other diastereoisomer), 5.09–5.05 (m, 1 H), 5.10–5.03 (m, 2 H), 4.72 (app. t, J = 6.6 Hz, 1 H), 3.77 (dq, J = 9.1, 7.1 Hz, 0.6 H, one diastereoisomer), 3.66 (q, J = 7.2 Hz, 1.3 H, other diastereoisomer), 3.61 (dq, J = 9.1, 7.2 Hz, 0.6 H, one diastereoisomer), 2.65–2.52 (m, 2 H), 2.57 (d, J = 1.8 Hz, 0.6 H, one diastereoisomer), 2.55 (d, J = 1.8 Hz, 0.3 H, other diastereoisomer), 1.25 (t, J = 7.1 Hz, 2 H, one diastereoisomer), 1.16 (t, J = 7.1 Hz, 1 H, other diastereoisomer) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.4 (C), 137.2 (CH), 132.0 (C), 131.7 (C), 130.6 (CH), 129.2 (CH), 116.5 (CH_2), 94.6 (CH), 78.6 (CH), 76.3 (CH), 73.4 (C), 59.9 (CH_2), 42.5 (CH_2), 15.1 (CH_3) ppm.

Compound 11a: Compound **11a** was prepared following the general procedure (starting from **8a**). Chromatography on silica gel (toluene/cyclohexane, 10:90) gave a 3:1 *anti*/*syn* mixture of **11a** in 72% yield as a colourless oil.

1-[1-(1-Ethoxyprop-2-ynyloxy)pent-4-enyl]benzene [*anti*-11a (*like*)]: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.18 (m, 5 H), 5.75 (ddt, J = 17.2, 10.4, 6.4 Hz, 1 H), 5.02 (d, J = 1.7 Hz, 1 H), 4.95 (ddd, J = 17.2, 3.2, 1.5 Hz, 1 H), 4.90 (dd, J = 10.1, 3.2 Hz, 1 H), 4.64 (dd, J = 7.6, 5.7 Hz, 1 H), 3.62 (qd, J = 7.1, 4.0 Hz, 2 H), 2.45 (d, J = 1.7 Hz, 1 H), 2.16–1.89 (m, 3 H), 1.73–1.66 (m, 1 H), 1.1 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.2 (C), 137.9 (C), 128.4 (2 CH), 127.7 (CH), 126.9 (2 CH), 114.8 (CH_2), 88.8 (CH), 79.2 (C), 77.3 (CH), 73.4 (CH), 59.6 (CH_2), 37.0 (CH_2), 29.9 (CH_2), 14.9 (CH_3) ppm. HRMS (ESI): calcd. for $C_{16}H_{20}Na_1O_2$ [M + Na]$^+$ 267.136; found 267.136.

1-[1-(1-Ethoxyprop-2-ynyloxy)pent-4-enyl]benzene [*syn*-11a (*unlike*)]: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.18 (m, 5 H), 5.75 (ddt, J = 17.2, 10.4, 6.4 Hz, 1 H maj + 0.5 H min), 5.12 (d, J = 1.7 Hz, 1 H maj), 5.02 (d, J = 1.7 Hz, 0.5 H min), 4.95 (ddd, J = 17.2, 3.2, 1.5 Hz, 1 H maj + 0.5 H min), 4.90 (dd, J = 10.1, 3.2 Hz, 1 H maj + 0.5 H min), 4.64 (dd, J = 7.6, 5.7 Hz, 0.5 H min), 4.54 (dd, J = 7.2, 5.7 Hz, 1 H maj), 3.69–3.56 (m, 2 × 0.5 H min + 1 H maj), 3.3 (dq, J = 9.3, 7.1 Hz, 1 H maj), 2.45 (d, J = 1.7 Hz, 0.5 H min), 2.44 (d, J = 1.7 Hz, 1 H maj), 2.16–1.89 (m, 3 × 0.5 H min, 3 H maj), 1.73–1.66 (m, 0.5 H min + 1 H maj), 1.1 (t, J = 7.1 Hz, 1.5 H min), 0.95 (t, J = 7.1 Hz, 3 H maj) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.1 (C maj), 141.2 (C min), 137.9 (C maj + C min), 128.4 (2 CH min), 128.3 (2 CH maj), 127.7 (CH min), 127.6 (CH maj), 126.9 (2CH min), 126.7 (2 CH maj), 114.9 (CH_2 maj), 114.8 (CH_2 min), 90.9 (CH maj), 88.8. (CH min), 79.3 (C min), 79.2 (C min), 78.8 (CH maj), 77.3 (CH min), 73.7 (CH maj), 73.4 (CH min), 61.3 (CH_2 maj), 59.6 (CH_2 min), 37.0 (CH_2 min), 36.8 (CH_2 maj), 29.9 (CH_2 min), 29.7 (CH_2 maj), 14.9 (CH_3 min), 14.6 (CH_3 maj) ppm.

Compound 11b: Compound **11b** was prepared following the general procedure (starting from **8b**). Chromatography on silica gel (toluene/cyclohexane, 10:90) gave a 3:2 *anti*/*syn* mixture of **11b** in 53% yield as a colourless oil.

3-[1-(1-Ethoxyprop-2-ynyloxy)pent-4-enyl]furan [*anti*-11b (*like*)]: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.37 (m, 2 H), 6.38 (d, J = 5.3 Hz, 1 H), 5.76 (ddt, J = 20.2, 10.2, 6.1 Hz, 1 H), 5.17 (d, J = 1.8 Hz, 1 H), 5.02 (d, J = 1.7 Hz, 1 H), 4.97–4.91 (m, 1 H), 4.66 (t, J = 6.7 Hz, 1 H), 3.74–3.60 (m, 2 H), 2.50 (d, J = 1.8 Hz, 1 H), 2.16–1.81 (m, 3 H), 1.75–1.68 (m, 1 H), 1.19 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.6 (CH), 140.7 (CH), 137.9 (CH), 125.3 (C), 114.9 (CH_2), 108.6 (CH), 88.4 (CH), 79.2 (C), 73.4 (CH), 69.2 (CH), 59.4 (CH_2), 35.5 (CH_2), 29.8 (CH_2),

15.0 (CH_3) ppm. HRMS (ESI): calcd. for $C_{14}H_{19}Na_1O_3$ [M + Na]$^+$ 257.115; found 257.122.

3-[1-(1-Ethoxyprop-2-ynyloxy)pent-4-enyl]furan [*syn*-11b (*unlike*)]: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.36 (m, 2 H), 7.19–7.07 (m, 1 H), 6.42 (s, 1 H), 5.58 (ddt, *J* = 17.2, 10.2, 6.4 Hz, 1 H), 5.28 (d, *J* = 1.8 Hz, 0.3 H, one diastereoisomer), 5.17 (dd, *J* = 7.3, 1.8 Hz, 0.65 H, one diastereoisomer), 5.06 (br. s, 0.65 H, other diastereoisomer), 5.00 (dd, *J* = 10.6, 1.8 Hz, 1.3 H, other diastereoisomer), 4.69 (t, *J* = 6.7 Hz, 0.65 H, one diastereoisomer), 4.66 (t, *J* = 6.7 Hz, 0.35 H, other diastereoisomer), 3.80–3.58 (m, 1.5 H), 3.46 (dq, *J* = 9.3, 7.1 Hz, 0.35 H, other diastereoisomer), 2.55 (d, *J* = 1.8 Hz, 0.65 H, one diastereoisomer), 2.53 (d, *J* = 1.8 Hz, 0.35 H, other diastereoisomer), 2.13–1.95 (m, 4 H), 1.85–1.75 (m, 2 H), 1.26 (t, *J* = 7.1 Hz, 1.95 H, one diastereoisomer), 1.14 (t, *J* = 7.1 Hz, 1.05 H, other diastereoisomer) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.6 (CH, *anti*), 143.3 (C, *syn*), 140.7 (CH, *anti*), 139.9 (CH, *syn*), 137.9 (CH, *syn* and *anti*), 125.3 (C, *anti*), 124.9 (C, *syn*), 115.0 (CH_2, *syn*), 114.9 (CH_2, *anti*), 108.8 (CH, *syn*), 108.6 (CH, *anti*), 90.6 (CH, *syn*), 88.4(CH, *anti*), 79.2 (C, *syn* and *anti*), 73.7 (CH, *syn*), 73.4 (CH, *anti*), 70.7 (CH, *syn*), 69.2 (CH, *anti*), 61.2 (CH_2, *syn*), 59.4 (CH_2, *anti*), 35.5 (CH_2, *anti*), 35.3 (CH_2, *syn*), 29.8 (CH_2, *anti*), 29.5 (CH_2, *syn*), 15.0 (CH_3, *anti*), 14.7 (CH_3, *syn*) ppm. HRMS (ESI): calcd. for $C_{14}H_{18}Na_1O_3$ [M + Na]$^+$ 257.115; found 257.119.

Compound 11e: This compound was prepared following the general procedure (starting from **8e**). Chromatography on silica gel (toluene/cyclohexane, 10:90) gave a 2:1 *anti*/*syn* mixture of **11e** in 66% yield as a colourless oil.

1,2-Dichloro-4-[1-(1-ethoxyprop-2-ynyloxy)pent-4-enyl]benzene [*anti*-11e (*like*)]: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 2.1 Hz, 1 H), 7.43 (d, *J* = 8.3 Hz, 1 H), 7.18 (dd, *J* = 8.3, 2.1 Hz, 1 H), 5.80 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1 H), 5.09 (d, *J* = 1.8 Hz, 1 H), 5.06–4.97 (m, 2 H), 4.69 (dd, *J* = 7.6, 5.7 Hz, 1 H), 3.66 (m, 2 H), 2.57 (d, *J* = 1.8 Hz, 1 H), 2.18–2.06 (m, 2 H), 2.02–1.91 (m, 1 H), 1.78–1.68 (m, 1 H), 1.16 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.0 (C), 137.6 (CH), 132.6 (C), 131.7 (C), 130.5 (CH), 130.5 (CH), 129.0 (CH), 115.2 (CH_2), 86.3 (CH), 78.8 (C), 76.0 (CH), 73.9 (CH), 60.1 (CH_2), 37.0 (CH_2), 29.8 (CH_2), 14.9 (CH_3) ppm. HRMS (ESI): calcd. for $C_{16}H_{19}Na_1Cl_2O_2$ [M + Na]$^+$ 335.058; found 335.058.

1,2-Dichloro-4-[1-(1-ethoxyprop-2-ynyloxy)pent-4-enyl]benzene [*syn*-11e (*unlike*)]: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 2.1 Hz, 1 H), 7.42 (d, *J* = 8.3 Hz, 1 H), 7.19 (dd, *J* = 8.3, 2.1 Hz, 1 H), 5.80 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1 H), 5.22 (d, *J* = 1.8 Hz, 1 H), 5.06–4.97 (m, 2 H), 4.62 (dd, *J* = 7.1, 5.8 Hz, 1 H), 3.74 (dq, *J* = 9.3, 7.1 Hz, 1 H), 3.41 (dq, *J* = 9.3, 7.1 Hz, 1 H), 2.52 (d, *J* = 1.8 Hz, 1 H), 2.18–2.05 (m, 2 H), 2.02–1.90 (m, 1 H), 1.78–1.69 (m, 1 H), 1.07 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.8 (C), 137.6 (CH), 132.4 (C), 131.4 (C), 130.3 (CH), 128.6 (CH), 126.0 (CH), 115.3 (CH_2), 91.1 (CH), 78.7 (C), 76.0 (CH), 74.3 (CH), 61.4 (CH_2), 36.9 (CH_2), 29.5 (CH_2), 14.7 (CH_3) ppm.

Compound 12a: Compound **12a** was prepared following the general procedure [starting from 3-methyl-1-phenylbut-3-en-1-ol (**9a**)]. Chromatography on silica gel (toluene/cyclohexane, 10:90) gave a 3:1 *anti*/*syn* mixture of **12a** in 51% yield as a colourless oil. R_f (mixture of diastereoisomers) = 0.6 (cyclohexane/Et_2O, 4:1, UV and vaniline).

1-[1-(1-Ethoxyprop-2-ynyloxy)-3-methylbut-3-enyl]benzene [*anti*-12a (*like*)]: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.28 (m, 5 H), 5.10 (d, *J* = 1.8 Hz, 1 H), 4.86 (dd, *J* = 7.9, 6.1 Hz, 1 H), 4.78 (br. q, *J* = 1.8 Hz, 1 H), 4.72 (br. q, *J* = 1.8 Hz, 1 H) 3.68 (q, *J* = 7.0 Hz, 2 H), 2.63 (dd, *J* = 13.9, 7.9 Hz, 1 H), 2.53 (d, *J* = 1.8 Hz, 1 H), 2.38 (dd, *J* = 13.9, 5.9 Hz, 1 H), 1.75 (s, 3 H), 1.17 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.8 (C), 141.2 (C), 128.4 (2 CH), 127.8 (CH), 127.1 (2 CH), 113.3 (CH_2), 88.9 (CH), 79.2 (C), 77.2 (CH), 76.8 (CH), 73.4 (C), 59.7 (CH_2), 46.2 (CH_2), 22.8 (CH_3), 14.9 (CH_3) ppm. HRMS (ESI): calcd. for $C_{16}H_{20}O_2Na$ [M + Na]$^+$ 267.136; found 267.131.

1-[1-(1-Ethoxyprop-2-ynyloxy)-3-methylbut-3-enyl]benzene [*syn*-12a (*unlike*)]: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.18 (m, 5 H), 5.21 (d, *J* = 1.8 Hz, 1 H), 4.79–4.70 (m, 3 H), 3.72 (dq, *J* = 9.3, 7.1 Hz, 1 H), 3.37 (dq, *J* = 9.3, 7.1 Hz, 1 H), 2.65 (dd, *J* = 14.0, 7.9 Hz, 1 H), 2.50 (d, *J* = 1.8 Hz, 1 H), 2.38 (dd, *J* = 14.2, 6.0 Hz, 1 H), 1.74 (s, 3 H), 1.03 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.0 (C), 141.7 (C), 128.2 (2 CH), 127.5 (CH), 126.7 (2 CH), 113.3 (CH_2), 90.8 (CH), 79.0 (C), 77.9 (CH), 76.8 (CH), 73.9 (C), 61.1 (CH_2), 46.2 (CH_2), 22.8 (CH_3), 14.6 (CH_3) ppm.

Compound 12b: This compound was prepared following the general procedure, starting from 3-methyl-1-phenylbut-3-en-1-ol (**9b**). Chromatography on silica gel (toluene/cyclohexane, 10:90) gave a 3:2 *anti*/*syn* mixture of **12b** in 42% yield as a colourless oil. R_f (mixture of diastereoisomers) = 0.5 (cyclohexane/Et_2O, 4:1, UV and *p*-anisaldehyde).

3-[1-(1-Ethoxyprop-2-ynyloxy)-3-methylbut-3-enyl]furan (12b): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.36 (m, 2 H), 6.43 (app. s, 1 H), 5.25 (d, *J* = 1.7 Hz, 0.4 H, one diastereoisomer), 5.20 (d, *J* = 1.8 Hz, 0.6 H, other diastereoisomer), 4.81–4.78 (m, 1 H), 4.76–4.73 (m, 1 H), 3.78–3.63 (m, 1.6 H), 3.49 (dq, *J* = 9.3, 7.0, 0.4 Hz, one diastereoisomer), 2.68–2.58 (m, 1 H), 2.55 (d, *J* = 1.7 Hz, 0.4 H, one diastereoisomer), 2.53 (d, *J* = 1.8 Hz, 0.6 H, other diastereoisomer), 2.44–2.35 (m, 1 H), 1.76 (s, 0.4 H, one diastereoisomer), 1.75 (d, 0.6 H, other diastereoisomer), 2.44–2.35 (m, 1 H), 1.21 (t, *J* = 7.1 Hz, 0.6 H, one diastereoisomer), 1.15 (t, *J* = 7.1 Hz, 0.6 H, other diastereoisomer) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.5, 143.1, 141.5, 140.6, 139.9, 125.9, 124.9, 113.4, 113.2, 108.9, 108.7, 90.6, 88.5, 79.1, 79.0, 73.8, 73.5, 69.8, 68.7, 61.1, 59.5, 44.8, 44.7, 22.7, 14.9, 14.8 ppm. HRMS (ESI): calcd. for $C_{14}H_{19}O_3Na$ [M + Na]$^+$ 257.115; found 257.114.

Enyne Metathesis

General Procedure for Enyne Ring-Closing Metathesis of Propargylic *O*,*O*-Acetals 5, 11 and 12: The enyne (0.15–0.2 mmol) and the Grubbs II or Grubbs I catalyst (2–5 mol-%) were dissolved in dichloroethane (0.1 M). Ethylene was bubbled through the mixture for 10 min whilst stirring at reflux. After the time indicated in Tables 2, 3 and 4 (GC monitoring), the reaction mixture was filtered through a charcoal pad, concentrated and then directly purified through a short column of silica (toluene/cyclohexane) to give the corresponding dienes. Alternatively, toluene could be used as solvent at 70 °C to give a similar conversion rate.

6-Ethoxy-2-phenyl-5-vinyl-3,6-dihydro-2*H*-pyran (*trans*-1a): (Table 2) ^{1}H NMR (300 MHz, C_6D_6): δ = 7.35–7.31 (m, 2 H), 7.19–7.06 (m, 3 H), 6.19 (dd, *J* = 17.7, 11.1 Hz, 1 H), 5.58 (dd, *J* = 5.6, 2.4 Hz, 1 H), 5.33 (s, 1 H), 5.26 (d, *J* = 17.8 Hz, 1 H), 5.04 (dd, *J* = 11.0, 3.6 Hz, 1 H), 4.99 (d, *J* = 11 Hz, 1 H), 3.75 (dq, *J* = 9.7, 7.1 Hz, 1 H), 3.37 (dq, *J* = 9.7, 7.1 Hz, 1 H), 2.17 (ddd, *J* = 18.2, 11.1, 2.1, 1.6 Hz, 1 H), 1.97 (ddd, *J* = 18.5, 5.7, 4.0 Hz, 1 H), 1.03 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 143.3 (C), 136.3 (CH), 135.1 (C), 128.9 (CH), 127.5 (C), 127.9 (CH), 126.6 (2 CH), 113.2 (CH_2), 96.4 (CH), 68.8 (CH), 63.8 (CH), 34.1 (CH_2), 15.9 (CH_3) ppm. HRMS (ESI): calcd. for $C_{15}H_{19}O_2Na$ [M + Na]$^+$ 253.120; found 253.121.

6-Ethoxy-2-phenyl-5-vinyl-3,6-dihydro-2*H*-pyran (*cis*-1a): (Table 2) ^{1}H NMR (300 MHz, C_6D_6): δ = 7.38–7.35 (m, 2 H), 7.22–7.08 (m, 3 H), 6.22 (dd, *J* = 17.7, 11.2 Hz, 1 H), 5.68 (dd, *J* = 6.3, 2.5 Hz, 1 H), 5.54 (app. t, *J* = 8.8 Hz, 1 H), 5.06 (d, *J* = 11.2 Hz, 1 H), 4.40 (dd, *J* = 10.3, 3.3 Hz, 1 H), 3.82 (dq, *J* = 9.4, 7.1 Hz, 1 H), 3.60 (dq, *J* = 9.4, 7.1 Hz, 1 H), 2.29–2.17 (m, 1 H), 1.90 (ddd, *J* = 17.8, 6.3, 3.3 Hz, 1 H), 1.16 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 143.0 (C), 137.0 (C), 135.6 (CH), 129.5 (CH), 128.8 (2 CH), 128.6 (CH), 127.9 (CH), 126.5 (2 CH), 114.5 (CH_2), 98.8 (CH), 73.59 (CH), 62.3 (CH_2), 33.9 (CH_2), 15.9 (CH_3) ppm. HRMS (ESI): calcd. for $C_{15}H_{19}O_2Na$ [M + Na]$^+$ 253.120; found 253.120.

6-Ethoxy-2-(furan-3-yl)-5-vinyl-3,6-dihydro-2*H*-pyran (*trans*-1b): (Table 2) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45 (m, 1 H), 7.42 (t, *J* = 1.7 Hz, 1 H), 6.45 (dd, *J* = 1.8, 0.9 Hz, 1 H), 6.28 (dd, *J* = 17.8, 10.9 Hz, 1 H), 5.98 (dd, *J* = 5.5, 2.7 Hz, 1 H), 5.29 (s, 1 H), 5.23 (d, *J* = 18.0 Hz, 1 H), 5.08 (d, *J* = 11.0 Hz, 1 H), 5.03 (dd, *J* = 11.0, 4.0 Hz, 1 H), 3.95 (dq, *J* = 9.8, 7.1 Hz, 1 H), 3.69 (dq, *J* = 9.8, 7.1 Hz, 1 H), 2.48 (dd, *J* = 18.5, 10.7 Hz, 1 H), 2.35 (ddd, *J* = 18.5, 5.6, 4.1 Hz, 1 H), 1.29 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.3 (CH), 139.3 (CH), 135.2 (CH), 135.1 (C), 128.2 (CH), 126.4 (C), 113.0 (CH_2), 108.9 (CH), 95.3 (CH), 63.5 (CH), 61.4 (CH_2), 31.6 (CH_2), 15.4 (CH_3) ppm. HRMS (ESI): calcd. for $C_{13}H_{16}O_3Na$ [M + Na]$^+$ 243.100; found 243.100.

6-Ethoxy-2-(furan-3-yl)-5-vinyl-3,6-dihydro-2*H*-pyran (*cis*-1b): (Table 2) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45 (m, 1 H), 7.39 (t, *J* = 1.8 Hz, 1 H), 6.46 (dd, *J* = 1.8, 0.9 Hz, 1 H), 6.25 (dd, *J* = 17.8, 11.2 Hz, 1 H), 6.08 (dd, *J* = 5.3, 2.8 Hz, 1 H), 5.52 (t, *J* = 2.5 Hz, 1 H), 5.38 (d, *J* = 18.0 Hz, 1 H), 5.08 (d, *J* = 11.4 Hz, 1 H), 4.71 (dd, *J* = 9.4, 4.0 Hz, 1 H), 3.83 (dq, *J* = 9.8, 7.1 Hz, 1 H), 3.65 (dq, *J* = 9.8, 7.1 Hz, 1 H), 2.57–2.47 (m, 1 H), 2.40–2.30 (m, 1 H), 1.22 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.0 (CH), 139.3 (CH), 136.0 (CH), 134.6 (C), 128.4 (CH), 126.5 (C), 114.1 (CH_2), 109.1 (CH), 97.5 (CH), 66.6 (CH), 62.4 (CH_2), 31.6 (CH_2), 15.2 (CH_3) ppm.

2-(3,4-Dichlorophenyl)-6-ethoxy-5-vinyl-3,6-dihydro-2*H*-pyran (1e): (Table 2) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70–7.48 (m, 1.5 H, mixture of diastereoisomers), 7.47–7.39 (m, 1.5 H, mixture of diastereoisomers), 7.25–7.20 (m, 2 H, mixture of diastereoisomers), 6.30 (dd, *J* = 17.7, 11.1 Hz, 1 H, maj), 6.25 (dd, *J* = 17.8, 11.1 Hz, 0.3 H, min), 6.09 (dd, *J* = 5.6, 3.2 Hz, 0.3 H, min), 5.99 (dd, *J* = 5.1, 2.9 Hz, 1 H, maj), 5.44 (s, 0.3 H, min), 5.33 (s, 1 H, maj), 5.26 (d, *J* = 17.7 Hz, 1 H, maj), 5.11 (d, *J* = 11.61 Hz, 1 H, mixture of diastereoisomers), 5.01 (dd, *J* = 10.0, 5.2 Hz, 1 H, maj), 4.23 (dd, *J* = 5.9, 3.8 Hz, 0.3 H, min), 3.90 (dq, *J* = 9.1, 7.1 Hz, 1 H, maj), 3.87 (dq, *J* = 9.1, 7.1 Hz, 0.3 H, min), 3.67 (dq, *J* = 9.1, 7.1 Hz, 1 H, maj), 2.43–2.33 (m, 2 H, mixture of diastereoisomers), 1.27 (t, *J* = 7.1 Hz, 3 H, maj), 1.25 (t, *J* = 7.1 Hz, 1 H, min) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.3 (C), 142.1 (C), 136.1 (CH), 135.2 (CH), 135.04 (CH), 132.5 (C), 131.4 (C), 130.4 (CH), 128.8 (C), 128.1 (C), 128.0 (CH), 127.8 (CH), 125.3 (CH), 125.2 (CH), 113.3 (CH_2), 98.1 (CH), 95.5 (CH), 77.2 (C), 68.1 (C), 67.0 (CH), 63.6 (CH), 62.5 (C), 32.8 (CH_2), 32.7 (CH_2), 15.3 (CH_3), 15.2 (CH_3) ppm. HRMS (ESI): calcd. for $C_{15}H_{16}Cl_2NaO_2Na$ [M + Na]$^+$ 321.04; found 321,00.

7-Ethoxy-2-phenyl-6-vinyl-2,3,4,7-tetrahydrooxepine (*trans*-14a): (Table 3) ^{1}H NMR (400 MHz, C_6D_6): δ = 7.42 (d, *J* = 8.0 Hz, 2 H), 7.22 (t, *J* = 7.7 Hz, 2 H), 7.11 (d, *J* = 7.4 Hz, 1 H), 6.28 (dd, *J* = 17.7, 11.2 Hz, 1 H), 5.69 (t, *J* = 5.6 Hz, 1 H), 5.62 (s, 1 H), 5.20 (d, *J* = 17.7 Hz, 1 H), 5.19 (dd, *J* = 7.5, 3.1 Hz, 1 H), 4.96 (d, *J* = 11.3 Hz, 1 H), 3.64 (dq, *J* = 9.6, 7.1 Hz, 1 H), 3.28 (dq, *J* = 9.6, 7.1 Hz, 1 H), 2.35–2.26 (m, 1 H), 2.16–2.08 (m, 1 H), 2.03–1.94 (m, 1 H), 1.89–1.81 (m, 1 H), 1.02 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 144.4 (C), 139.7 (C), 138.8 (CH), 131.31 (CH), 126.95 (CH), 126.08 (CH), 114.6 (CH_2), 99.5 (CH), 72.6 (CH), 63.8 (CH_2), 36.9 (CH_2), 24.9 (CH_2), 14.9 (CH_3) ppm. HRMS (ESI): calcd. for $C_{16}H_{22}O_2$ [M + H]$^+$ 245.154; found 245.156.

7-Ethoxy-2-phenyl-6-vinyl-2,3,4,7-tetrahydrooxepine (*cis*-14a): (Table 3) ^{1}H NMR (400 MHz, C_6D_6): δ = 7.35 (d, *J* = 7.5 Hz, 2 H), 7.21 (t, *J* = 7.5 Hz, 2 H), 7.11 (d, *J* = 7.6 Hz, 1 H), 6.44 (dd, *J* = 18.0, 10.8 Hz, 1 H), 5.81 (t, *J* = 7.0 Hz, 1 H), 5.37 (d, *J* = 17.5 Hz, 1 H), 5.32 (s, 1 H), 5.01 (d, *J* = 11.6 Hz, 1 H), 4.45 (dd, *J* = 8.6, 5.4 Hz, 1 H), 3.85 (dq, *J* = 9.4, 7.0 Hz, 1 H), 3.38 (dq, *J* = 9.4, 7.0 Hz, 1 H), 2.63–2.52 (m, 1 H), 2.09–2.00 (m, 1 H), 1.88–1.73 (m, 2 H), 1.12 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 144.4 (C), 139.9 (C), 138.7 (CH), 131.3 (CH), 126.95 (CH), 126.08 (CH), 115.0 (CH_2), 101.6 (CH), 78.5 (CH), 61.4 (CH_2), 37.5 (CH_2), 24.9 (CH_2), 15.5 (CH_3) ppm.

1-[1-(1-Ethoxy-2-methylenebut-3-enyloxy)pent-4-enyl]benzene (15a): (Table 3) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.25 (m, 5 H), 6.73 (dd, *J* = 18.1, 11.4 Hz, 1 H), 6.41 (d, *J* = 8.6 Hz, 1 H), 5.31–4.65 (m, 6 H), 4.60 (t, *J* = 6.9 Hz, 1 H), 3.90 (qd, *J* = 7.1, 5.8 Hz, 2 H), 2.49–2.21 (m, 2 H), 2.05–1.83 (m, 2 H), 1.32–1.23 (m, 3 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 145.6 (CH), 145.05 (CH), 143.9 (C), 142.5 (C), 129.3 (CH), 129.3 (CH), 128.4 (CH), 128.3 (CH), 127.3 (CH), 127.0 (CH), 126.0 (CH), 125.5 (CH), 12.0 (CH_2), 111.8 (CH_2), 111.4 (CH_2), 80.7 (CH), 80.5 (CH), 78.2 (CH), 78 (CH), 68.6 (CH_2), 36.32 (CH_2), 35.2 (CH_2), 34.0 (CH_2), 32.8 (CH_2), 31.8 (CH_2), 15.4 (CH_3), 15.3 (CH_3) ppm.

7-Ethoxy-2-(furan-3-yl)-6-vinyl-2,3,4,7-tetrahydrooxepine (*trans*-14b): (Table 3) ^{1}H NMR (400 MHz, C_6D_6): δ = 7.35 (s, 1 H), 7.13 (t, *J* = 1.6 Hz, 1 H), 6.25 (dd, *J* = 17.7, 11.1 Hz, 1 H), 6.24 (s, 1 H), 5.67 (t, *J* = 5.7 Hz, 1 H), 5.53 (s, 1 H), 5.16 (d, *J* = 17.7 Hz, 1 H), 5.11 (t, *J* = 14.3 Hz, 1 H), 4.94 (d, *J* = 11.0 Hz, 1 H), 3.69 (dq, *J* = 9.6, 7.1 Hz, 1 H), 3.31 (dq, *J* = 9.7, 7.1 Hz, 1 H), 2.33–2.21 (m, 1 H), 2.08–1.96 (m, 2 H), 1.82–1.74 (m, 1 H), 1.05 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 143.5 (CH), 140.3 (C), 139.6 (CH), 139.3 (CH), 134.1 (CH), 129.2 (C), 121.7 (CH), 111.8 (CH_2), 109.7 (CH), 99.8 (CH), 67.2 (CH), 64.5 (CH_2), 36.0 (CH_2), 25.3 (CH_2), 15.6 (CH_3) ppm. HRMS (ESI): calcd. for $C_{14}H_{18}Na_1O_3$ [M + H]$^+$ 257.115; found 257.120.

7-Ethoxy-2-(furan-3-yl)-6-vinyl-2,3,4,7-tetrahydrooxepine (*cis*-14b): (Table 3) ^{1}H NMR (400 MHz, C_6D_6): δ = 7.25 (s, 1 H), 7.11 (t, *J* = 1.6 Hz, 1 H), 6.41 (dd, *J* = 17.8, 11.0 Hz, 1 H), 6.23 (s, 1 H), 5.78 (t, *J* = 6.3 Hz, 1 H), 5.34 (d, *J* = 17.8 Hz, 1 H), 5.30 (s, 1 H), 4.99 (d, *J* = 11.0 Hz, 1 H), 4.37 (dd, *J* = 8.8, 5.1 Hz, 1 H), 3.80 (dq, *J* = 9.3, 7.1 Hz, 1 H), 3.36 (dq, *J* = 9.0, 7.2 Hz, 1 H), 2.51–2.41 (m, 1 H), 1.91–1.79 (m, 2 H), 1.66–1.55 (m, 1 H), 1.09 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 143.5 (CH), 140.9 (C), 139.3 (CH), 137.7 (CH), 131.8 (CH), 128.7 (CH), 127.7 (C), 112.8 (CH_2), 109.8 (CH), 102.8 (CH), 71.1 (CH), 64.0 (CH_2), 34.0 (CH_2), 24.7 (CH_2), 15.7 (CH_3) ppm. HRMS (ESI): calcd. for $C_{14}H_{18}Na_1O_3$ [M + H]$^+$ 257.115; found 257.118.

Signals of trace amounts of compound **15b** were observed in the NMR spectra of **14b**.

2-(3,4-Dichlorophenyl)-7-ethoxy-6-vinyl-2,3,4,7-tetrahydrooxepine (*trans*-14e): (Table 3) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 2.0 Hz, 1 H), 7.39 (d, *J* = 8.3 Hz, 1 H), 7.19 (dd, *J* = 8.3, 2.0 Hz, 1 H), 6.25 (dd, *J* = 17.7, 11.2 Hz, 1 H), 5.91 (t, *J* = 5.7 Hz, 1 H), 5.52 (s, 1 H), 5.11 (d, *J* = 17.8 Hz, 1 H), 5.07 (dd, *J* = 7.2, 3.9 Hz, 1 H), 4.99 (d, *J* = 11.2 Hz, 1 H), 3.72 (dq, *J* = 9.8, 7.1 Hz, 1 H), 3.55 (dq, *J* = 9.6, 7.1 Hz, 1 H), 2.51–2.38 (m, 1 H), 2.33–2.19 (m,

4 H), 1.93–1.83 (m, 1 H), 1.22 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 144.1 (C), 138.8 (C), 138.1 (CH), 133.7 (CH), 133.8 (C), 130.8 (C), 128.0 (CH), 125.3 (CH), 111.7 (CH_2), 99.2 (CH), 71.6 (CH), 64.2 (CH_2), 36.3 (CH_2), 29.7 (CH_2), 24.8 (CH_2), 15.06 (CH_3) ppm. HRMS (ESI): calcd. for $C_{16}H_{19}Cl_2NaO_2$ [M + Na]$^+$ 335.058; found 335.063.

2-(3,4-Dichlorophenyl)-7-ethoxy-6-vinyl-2,3,4,7-tetrahydrooxepine (*cis*-14e): (Table 3) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 2.0 Hz, 1 H), 7.39 (d, *J* = 8.3 Hz, 1 H), 7.19 (dd, *J* = 8.3, 2.0 Hz, 1 H), 6.31 (dd, *J* = 17.7, 11.2 Hz, 1 H), 5.64 (s, 1 H), 5.48 (t, *J* = 5.7 Hz, 1 H), 5.34 (d, *J* = 17.8 Hz, 1 H), 4.99 (d, *J* = 11.2 Hz, 1 H), 4.47 (dd, *J* = 7.2, 3.9 Hz, 1 H), 3.80 (dq, *J* = 9.7, 7.1 Hz, 1 H), 3.36 (dq, *J* = 9.7, 7.1 Hz, 1 H), 2.51–2.38 (m, 1 H), 2.33–2.19 (m, 4 H), 1.93–1.83 (m, 1 H), 1.10 (t, *J* = 7.1 Hz, 1 H) ppm.

1,2-Dichloro-4-[1-[1-ethoxy-2-methylenebut-3-enyloxy)pent-4-enyl]-benzene (15e): (Table 3) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 2.0 Hz, 1 H), 7.39 (d, *J* = 8.3 Hz, 1 H), 7.16 (ddd, *J* = 13.6, 8.3, 2.0 Hz, 1 H), 6.28 (dd, *J* = 17.8, 11.2 Hz, 1 H), 5.82 (mc, 1 H), 5.47–5.41 (m, 2 H), 5.29 (s, 1 H), 5.11–4.97 (m, 4 H), 4.71 (t, *J* = 6.9 Hz, 1 H), 3.45 (dq, *J* = 9.4, 7.1 Hz, 1 H), 3.33 (dq, *J* = 9.4, 7.1 Hz, 1 H), 2.14–2.07 (m, 2 H), 2.05–1.73 (m, 2 H), 1.32–1.14 (m, 3 H) ppm.

6-Ethoxy-4-methyl-2-phenyl-5-vinyl-3,6-dihydro-2*H*-pyran (*trans*-16a): (Table 4) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.30 (m, 5 H), 6.72 (dd, *J* = 17.7, 11.4 Hz, 1 H), 5.33 (s, 1 H), 5.26 (d, *J* = 17.7 Hz, 1 H), 5.18–5.08 (m, 2 H), 3.92 (dq, *J* = 9.7, 7.1 Hz, 1 H), 3.65 (dq, *J* = 9.7, 7.1 Hz, 1 H), 2.45 (dd, *J* = 18.2, 11.5 Hz, 1 H), 2.23 (dd, *J* = 18.2, 4.2 Hz, 1 H), 1.87 (s, 3 H), 1.27 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.0 (C), 134.5 (C), 131.0 (CH), 128.4 (2 CH), 127.9 (C), 127.5 (CH), 126.0 (2 CH), 113.0 (CH_2), 96.0 (CH), 68.0 (CH), 63.2 (CH_2), 39.1 (CH_2), 18.6 (CH_3), 15.4 (CH_3) ppm. HRMS (ESI): calcd. for $C_{16}H_{20}NaO_2$ [M + Na]$^+$ 267.136; found 267.136.

1-[(1-Ethoxy-2-methylenebut-3-enyloxy)-3-methylbut-3-enyl]benzene (*trans*-17a): (Table 4) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.28 (m, 5 H), 6.32 (dd, *J* = 17.6, 11.1 Hz, 1 H), 5.54 (dd, *J* = 17.8, 1.6 Hz, 1 H), 5.33 (m, 2 H), 5.12 (d, *J* = 11.4 Hz, 1 H), 4.94 (s, 1 H), 4.71 (br. s, 1 H), 4.63 (br. s, 1 H), 4.51 (t, *J* = 6.9 Hz, 1 H), 3.49 (dq, *J* = 9.5, 7.0 Hz, 1 H), 3.19 (dq, *J* = 9.5, 7.0 Hz, 1 H), 2.64 (dd, *J* = 13.9, 7.6 Hz, 1 H), 2.38 (dd, *J* = 13.9, 6.3 Hz, 1 H), 1.66 (s, 3 H), 0.99 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.4 (C), 141.9 (C), 134.4 (C), 128.2 (CH), 128.1 (2 CH), 127.5 (CH), 127.0 (2 CH), 116.9 (CH_2), 115.8 (CH_2), 113.4 (CH_2), 100.4 (CH), 77.2 (CH), 61.4 (CH_2), 46.3 (CH_2), 22.9 (CH_3), 14.9 (CH_2) ppm. MS (ESI): calcd. for $C_{18}H_{24}NaO_2$ [M + Na]$^+$ 295.37; found 267.38.

6-Ethoxy-2-(furan-3-yl)-4-methyl-5-vinyl-3,6-dihydro-2*H*-pyran (*trans*-16b): (Table 4) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46 (m, *J* = 1.4 Hz, 1 H), 7.42 (d, *J* = 1.9 Hz, 1 H), 6.70 (dd, *J* = 17.7, 11.3 Hz, 1 H), 6.45 (d, *J* = 1.9 Hz, 1 H), 5.26 (s, 1 H), 5.17 (d, *J* = 17.6 Hz, 1 H), 5.11–5.04 (m, 2 H), 3.93 (dq, *J* = 9.8, 7.1 Hz, 1 H), 3.66 (dq, *J* = 9.8, 7.1 Hz, 1 H), 2.50–2.45 (m, 1 H), 2.24–2.15 (m, 1 H), 1.87 (s, 3 H), 1.30 (t, *J* = 7.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.0 (C), 139.3 (C), 134.1 (C), 132.5 (CH), 131.0 (CH), 113.0 (CH_2), 108.9 (CH), 96.0 (CH), 68.2 (CH), 63.2 (CH_2), 43.4 (CH_2), 18.6 (CH_3), 15.4 (CH_3) ppm. MS (ESI): calcd. for $C_{14}H_{18}NaO_3$ [M + Na]$^+$ 257.11; found 257.22.

3-[1-(1-Ethoxy-2-methylenebut-3-enyloxy)-3-methylbut-3-enyl]furan (*anti*-17b): (Table 4) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37 (app. s, 2 H), 6.38 (app. s, 1 H), 6.28 (dd, *J* = 17.8, 11.3 Hz, 1 H), 5.45 (d, *J* = 17.8 Hz, 1 H), 5.40 (app. s, 1 H), 5.26 (s, 1 H), 5.07 (d, *J* = 11.3 Hz, 1 H), 5.01 (app. s, 1 H), 4.90 (t, *J* = 7.0 Hz, 1 H), 4.76 (app. d, *J* = 11.9 Hz, 2 H), 3.45 (dq, *J* = 9.2, 7.0 Hz, 1 H), 3.34 (dq, *J* = 9.2, 7.0 Hz, 1 H), 2.62 (dd, *J* = 14.2, 7.0 Hz, 1 H), 2.40 (dd, *J* = 14.2, 7.0 Hz, 1 H), 1.76 (s, 3 H), 1.17 (t, *J* = 7.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.2 (CH), 142.9 (C), 140.4 (C), 135.0 (CH), 125.6 (C), 117.1 (CH_2), 115.3 (CH_2), 113.1 (CH_2), 108.96 (CH), 97.28 (CH), 68.4 (CH), 59.1 (CH_2), 45.06 (CH_3), 29.6 (CH_3) ppm.

3-[1-(1-Ethoxy-2-methylenebut-3-enyloxy)-3-methylbut-3-enyl]furan [*antilsyn*-17b (1:1)]: (Table 4) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.35 (m, 2 H), 6.45 (app. s, 0.5 H, one diastereoisomer), 6.38 (app. s, 0.5 H, other diastereoisomer), 6.29 (dd, *J* = 18.8, 10.9 Hz, 0.5 H, one diastereoisomer), 6.28 (dd, *J* = 17.8, 11.3 Hz, 0.5 H, other diastereoisomer), 5.54 (d, *J* = 17.8 Hz, 0.5 H, one diastereoisomer), 5.45 (d, *J* = 17.8 Hz, 0.5 H, other diastereoisomer), 5.40 (app. s, 0.5 H, one diastereoisomer), 5.33 (d, *J* = 12.2 Hz, 0.5 H, other diastereoisomer), 5.26 (s, 0.5 H, one diastereoisomer), 5.13 (d, *J* = 11.0 Hz, 0.5 H, one diastereoisomer), 5.07 (d, *J* = 11.3 Hz, 0.5 H, other diastereoisomer), 5.01 (app. s, 0.5 H, one diastereoisomer), 5.00 (app. s, 0.5 H, other diastereoisomer), 4.90 (t, *J* = 7.0 Hz, 0.5 H, one diastereoisomer), 4.76–4.68 (m, 2 H), 4.55 (t, *J* = 7.0 Hz, 0.5 H, other diastereoisomer), 3.54 (dq, *J* = 9.4, 7.0 Hz, 0.5 H, one diastereoisomer), 3.45 (dq, *J* = 9.2, 7.0 Hz, 0.5 H, other diastereoisomer), 3.34 (dq, *J* = 9.2, 7.0 Hz, 0.5 H, one diastereoisomer), 3.32 (dq, *J* = 9.2, 7.0 Hz, 0.5 H, other diastereoisomer), 2.62 (dd, *J* = 14.2, 7.0 Hz, 1 H), 2.40 (dd, *J* = 14.2, 7.0 Hz, 1 H), 1.76 (s, 1.5 H, one diastereoisomer), 1.70 (s, 1.5 H, other diastereoisomer), 1.17 (t, *J* = 7.0 Hz, 1.5 H, one diastereoisomer), 1.17 (t, *J* = 7.0 Hz, 1.5 H, other diastereoisomer) ppm.

Synthesis of Enynes 18 and 20

General Procedure for Alkylation (G3): Enynes **18** and **20** were prepared by Snapper and co-workers' modified procedure.[11b] The alcohol (1 equiv.) was added neat through a syringe to a flask charged with NaH (1.5 equiv.) in THF (0.5 M) at 0 °C with vigorous stirring (5 mmol scale). The mixture was warmed to room temp. and stirred for 1 h before cooling to 0 °C. 15-Crown-5 (1 equiv.) was added slowly and the reaction mixture was stirred for 0.5 h at room temp. After cooling again to 5 °C, neat propargyl bromide (3 equiv.) was added and the reaction mixture was stirred for 2 h to completion. The reaction was quenched with ice–water and diethyl ether. The aqueous layer was extracted with diethyl ether and the combined organics washed with sat. $Na_2S_2O_3$, water and brine, dried with $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by short-column silica gel chromatography afforded the enynes as oils.

1-(Prop-2-ynyloxy)pent-4-enylbenzene (18a): Compound **18a** was prepared following the general experimental procedure G3 starting from **8a**. Purification by flash chromatography gave 1-(prop-2-ynyloxy)pent-4-enylbenzene (**18a**) as a yellow oil (89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.23–7.18 (m, 5 H), 5.83 (ddt, *J* = 17.1, 10.3, 6.6 Hz, 1 H), 5.03 (ddd, *J* = 17.1, 3.3, 1.7 Hz, 1 H), 4.98 (ddd, *J* = 10.4, 3.3, 1.7 Hz, 1 H), 4.85 (d, *J* = 16 Hz, 1 H), 4.49 (d, *J* = 7.7, 5.7 Hz, 1 H, 1 H), 4.11 (dd, *J* = 15.5, 2.4 Hz, 1 H), 3.85 (dd, *J* = 15.5, 2.4 Hz, 1 H), 2.41 (t, *J* = 2.4 Hz, 1 H), 2.21–2.05 (m, 2 H), 2.02–1.90 (m, 1 H), 1.75 (ddt, *J* = 13.4, 9.2, 6.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.1 (C), 138.1 (CH), 128.5 (2 CH), 128.1 (C), 127.8 (CH), 126.9 (2 CH), 114.8 (CH_2), 80.2 (CH), 80.0 (C), 73.9 (CH), 55.6 (CH_2), 36.9 (CH_2), 29.9 (CH_2) ppm. HRMS (ESI): calcd. for $C_{14}H_{16}K_1O$ [M + K]$^+$ 239.083; found 239.104.

3-[1-(Prop-2-ynyloxy)pent-4-enyl]furan (18b): Compound **18b** was prepared following the general experimental procedure G3 starting from **8b**. Purification by flash chromatography (toluene/cyclohexane, 50:50) gave 1-(prop-2-ynyloxy)pent-4-enylbenzene (**18b**) as a yellow oil (84%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.38 (m, 2 H), 6.37 (app. s, 1 H), 5.82 (ddt, J = 17.1, 10.3, 6.6 Hz, 1 H), 5.2 (ddd, J = 17.0, 3.2, 1.6 Hz, 1 H), 4.97 (ddd, J = 10.3, 3.2, 1.6 Hz, 1 H), 4.50 (t, J = 6.7 Hz, 1 H), 4.12 (dd, J = 15.6, 2.4 Hz, 1 H), 3.91 (dd, J = 15.6, 2.4 Hz, 1 H), 2.39 (t, J = 2.4 Hz, 1 H), 2.18–2.06 (m, 2 H), 2.02–1.90 (m, 1 H), 1.79–1.68 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.6 (CH), 149.7 (CH), 137.9 (CH), 124.9 (C), 114.9 (CH_2), 108.5 (CH), 80.05 (CH), 74.0 (C), 71.8 (CH), 55.13 (CH_2), 35.3 (CH_2), 29.8 (CH_2) ppm. HRMS (ESI): calcd. for $C_{12}H_{14}Na_1O_2$ $[M + Na]^+$ 229.084; found 229.083.

1-[3-Methyl-1-(prop-2-ynyloxy)but-3-enyl]benzene (20a): Compound **20a** was prepared following the general experimental procedure G3 starting from **9a**. Purification by flash chromatography (toluene/cyclohexane, 50:50) gave 3-methyl-1-(prop-2-ynyloxy)but-3-enylbenzene (**20a**) as a yellow oil (71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.18 (m, 5 H), 4.78 (d, J = 11.5 Hz, 1 H), 4.71 (dd, J = 8.4, 5.4 Hz, 1 H), 4.14 (dd, J = 15.8, 2.5 Hz, 1 H), 3.85 (dd, J = 15.8, 2.5 Hz, 1 H), 2.62 (dd, J = 14.4, 8.4 Hz, 1 H), 2.41 (t, J = 2.4 Hz, 1 H), 2.36 (dd, J = 14.4, 5.3 Hz, 1 H), 1.76 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.6 (C), 140.4 (C), 128.4 (2 CH), 127.7 (CH), 126.9 (2 CH), 117.0 (CH_2), 80.3 (CH), 79.6 (C), 74.2 (CH), 55.7 (CH_2), 42.1 (CH_2), 22.4 (CH_3) ppm. HRMS (ESI): calcd. for $C_{14}H_{16}KO$ $[M + K]^+$ 239.083; found 239.103.

3-[3-Methyl-1-(prop-2-ynyloxy)but-3-enyl]furan (20b): Compound **20b** was prepared following the general experimental procedure G3 starting from **9b**. Purification by flash chromatography (toluene/cyclohexane, 50:50) gave 3-[3-methyl-1-(prop-2-ynyloxy)but-3-enyl]furan (**20b**) as a yellow oil (71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.40 (m, 2 H), 6.41 (app. s, 1 H), 4.78 (d, J = 11.6 Hz, 1 H), 4.72 (dd, J = 7.9, 6.1 Hz, 1 H), 4.15 (dd, J = 15.8, 2.4 Hz, 1 H), 3.93 (dd, J = 15.9, 2.4 Hz, 1 H), 2.63 (dd, J = 14.3, 7.9 Hz, 1 H), 2.41 (t, J = 2.4 Hz, 1 H), 2.38 (dd, J = 14.5, 6.4 Hz, 1 H), 1.76 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.5 (CH), 141.8 (C), 140.7 (CH), 124.7 (C), 112.9 (CH_2), 108.7 (CH), 79.8 (C), 74.1 (C), 70.6 (CH), 55.01 (CH_2), 44.5 (CH_2), 22.6 (CH_3) ppm. HRMS (ESI): calcd. for $C_{12}H_{14}K_1O_2$ $[M + K]^+$ 229.063; found 229.170.

2-Phenyl-6-vinyl-2,3,4,7-tetrahydrooxepine (19a): Compound **19a** was prepared following the general experimental procedure for the metathesis starting from **18a**. After the time indicated in Scheme 4 (GC monitoring), the reaction mixture was concentrated and then directly purified through a short column of silica (toluene/cyclohexane) to give **19a** in 86%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.23 (m, 5 H), 6.33 (dd, J = 17.9, 11.1 Hz, 1 H), 5.94 (t, J = 5.5 Hz, 1 H), 5.02 (d, J = 17.8 Hz, 1 H), 4.95 (d, J = 11.0 Hz, 1 H), 4.80 (dd, J = 7.8, 5.2 Hz, 1 H), 4.69 (d, J = 15.5 Hz, 1 H), 4.35 (d, J = 15.5, 1.8 Hz, 1 H), 2.60–2.47 (m, 1 H), 2.40–2.19 (m, 2 H), 2.02–1.90 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.4 (C), 138.9 (C), 137.3 (CH), 133.7 (CH), 127.2 (2 CH), 126.2 (CH), 124.9 (CH), 109.5 (CH_2), 81.5 (CH), 64.7 (CH_2), 33.8 (CH_2), 24.0 (CH_2) ppm. HRMS (ESI): calcd. for $C_{14}H_{16}K_1O_1$ $[M + K]^+$ 239.083; found 239.101.

2-(Furan-3-yl)-6-vinyl-2,3,4,7-tetrahydrooxepine (19b): Compound **19b** was prepared following the general experimental procedure for the metathesis starting from **18b**. After the time indicated in Scheme 4 (GC monitoring), the reaction mixture was concentrated and then directly purified through a short column of silica (toluene/cyclohexane) to give **19b** in 75%. ^{1}H NMR (300 MHz, C_6D_6): δ = 7.08 (dd, J = 2.3, 1.2 Hz, 1 H), 6.95 (t, J = 1.7 Hz, 1 H), 6.08 (s, 1 H), 6.06 (dd, J = 18.0, 11.2 Hz, 1 H), 5.49 (t, J = 5.8 Hz, 1 H), 4.68 (d, J = 10.9 Hz, 1 H), 4.63 (d, J = 4.3 Hz, 1 H), 4.37 (dd, J = 7.7, 5.2 Hz, 1 H), 4.33 (d, J = 14.9 Hz, 1 H), 3.97 (dq, J = 15.5, 1.5 Hz, 1 H), 2.03–1.83 (m, 2 H), 1.65–1.47 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.1 (CH), 142.3 (C), 140.3 (C), 139.5 (CH), 138.8 (CH), 133.7 (2 CH), 128.8 (CH), 110.4 (CH_2), 109.6 (CH), 75.3 (CH), 64.6 (CH_2), 33.9 (CH_2), 25.03 (CH_2) ppm. HRMS (ESI): calcd. for $C_{12}H_{14}Na_1O_3$ $[M + Na + O]^+$ 229.084; found 239.091.

4-Methyl-2-phenyl-5-vinyl-3,6-dihydro-2*H*-pyran (21a): Compound **21a** was prepared following the general experimental procedure for the metathesis starting from **20a**. After the time indicated in Scheme 5 (monitored by GC), the reaction mixture was concentrated and then directly purified through a short column of silica (toluene/cyclohexane = 50:50) to give **21a** and **22a** in 46 and 30% yields, respectively. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.23 (m, 5 H), 6.76 (dd, J = 17.7, 11.5 Hz, 1 H), 5.04 (d, J = 4.0 Hz, 1 H), 4.99 (d, J = 10.4 Hz, 1 H), 2.49–2.41 (m, 1 H), 2.24 (dt, J = 17.4, 2.6 Hz, 2 H), 1.86 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.3 (C), 131.2 (CH), 130.8 (C), 128.3 (2 CH), 127.5 (CH), 125.8 (2 CH), 111.0 (CH_2), 75.8 (CH), 66.4 (CH_2), 39.3 (CH_2), 18.4 (CH_3) ppm. HRMS (ESI): calcd. for $C_{14}H_{16}Li_1O_1$ $[M + Li]^+$ 207.136; found 207.139.

1-[3-Methyl-1-(2-methylenebut-3-enyloxy)but-3-enyl]benzene (22a): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.28 (m, 5 H), 6.36 (dd, J = 17.8, 11.0 Hz, 1 H), 5.25 (d, J = 5.6 Hz, 1 H), 5.17 (d, J = 5.6 Hz, 1 H), 5.05 (d, J = 11.3 Hz, 1 H), 4.76 (d, J = 1.9 Hz, 1 H), 4.07 (d, J = 1.9 Hz, 1 H), 4.46 (dd, J = 8.0, 5.6 Hz, 1 H), 4.10 (d, J = 12.6 Hz, 1 H), 3.91 (d, J = 13.2 Hz, 1 H), 2.60 (dt, J = 14.1, 8.0 Hz, 1 H), 2.34 (dd, J = 14.2, 5.5 Hz, 1 H), 1.73 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.6 (C), 142.4 (C), 142.2 (C), 136.6 (CH), 128.32 (2 CH), 127.54 (2 CH), 111.1 (CH_2), 114.2 (CH_2), 112.8 (CH_2), 80.5 (CH), 68.0 (CH_2), 46.7 (CH_2), 22.9 (CH_3) ppm.

2-(Furan-3-yl)-4-methyl-5-vinyl-3,6-dihydro-2*H*-pyran (21b): Compound **21b** was prepared following the general experimental procedure for the metathesis starting from **20b**. After the time indicated in Scheme 5 (monitored by GC), the reaction mixture was concentrated and then directly purified through a short column of silica (toluene/cyclohexane = 50:50) to give **21b** and **22b** in 32 and 45% yields, respectively. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43 (m, 1 H), 7.41 (t, J = 1.7 Hz, 1 H), 6.76 (dd, J = 17.8, 11.3 Hz, 1 H), 6.45 (dd, J = 1.9, 0.9 Hz, 1 H), 6.45 (dd, J = 2.3, 1.3 Hz, 1 H), 5.02 (d, J = 6.7 Hz, 1 H), 4.97 (d, J = 13.6 Hz, 1 H), 4.56 (dd, J = 10.2, 3.7 Hz, 1 H), 4.38 (dq, J = 14.8, 2.1 Hz, 1 H), 2.57–2.42 (m, 1 H), 2.22 (dt, J = 17.2, 2.6 Hz, 2 H), 1.86 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.2 (CH), 139.2 (CH), 131.2 (CH), 130.2 (C), 126.9 (C), 126.6 (C), 111.0 (CH_2), 108.6 (CH), 68.6 (CH), 65.8 (CH_2), 37.7 (CH_2), 18.4 (CH_3) ppm.

3-[3-Methyl-1-(2-methylenebut-3-enyloxy)but-3-enyl]furan (22b): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41 (t, J = 1.8 Hz, 1 H), 7.37 (s, 2 H), 6.44 (d, J = 1.8 Hz, 1 H), 6.36 (dd, J = 17.79, 11.0 Hz, 1 H), 5.65 (d, J = 7.5 Hz, 1 H), 5.23 (d, J = 9.3 Hz, 1 H), 5.21 (s, 1 H), 5.07 (d, J = 11.0 Hz, 1 H), 4.75 (dt, J = 17.2, 1.9 Hz, 1 H), 4.47 (t, J = 7.0 Hz, 1 H), 4.15 (d, J = 12.5 Hz, 1 H), 3.96 (d, J = 12.6 Hz, 1 H), 2.62 (dd, J = 14.0, 7.5 Hz, 1 H), 2.37 (dd, J = 14.0, 6.4 Hz, 1 H), 1.73 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.3 (CH), 142.6 (C), 142.1 (C), 140.2 (CH), 136.6 (CH), 125.9 (CH), 117.3 (CH_2), 114.4 (CH_2), 112.9 (CH_2), 108.8 (C), 72.0 (CH), 67.7 (CH_2), 44.9 (CH_2), 22.8 (CH_3) ppm.

Supporting Information (see also footnote on the first page of this article): Experimental procedure for the preparation of cycloadducts **24** and **26**, full analytical data for compounds **5c**, **5d**, **6**, **7a**, **7b**, **8a**, **8b**, **9a**, **10**, **24** and **26** and ^{1}H and ^{13}C NMR spectra for **6**–**26**.

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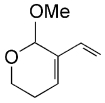

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