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Ring closing metathesis of prochiral oxaenediynes to racemic 4-alkenyl-2-alkynyl-3,6-dihydro-2*H*-pyrans

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Abstract

Prochiral 4-(allyloxy)hepta-1,6-diynes, optionally modified in the positions 1 and 7 with an alkyl or ester group, undergo chemoselective ring closing enyne metathesis yielding racemic 4-alkenyl-2-alkynyl-3,6-dihydro-2*H*-pyrans. Among the catalysts tested, Grubbs 1st generation precatalyst in the presence of ethene (Mori conditions) gave superior results compared to more stable Grubbs or Hoveyda-Grubbs 2nd generation precatalysts. This is probably caused by suppression of subsequent side-reactions of the enyne metathesis product with ethene. On the other hand, 2nd generation precatalysts gave better yields in the absence of ethene. The metathesis products, containing both triple bond and conjugated system, can be successfully orthogonally modified. For example, metathesis product of 5-(allyloxy)nona-2,7-diyne reacted chemo- and stereoselectively by Diels-Alder reaction with *N*-phenylmaleimide affording tricyclic products as the mixture of two separable diastereoisomers, the

configuration of which was estimated by DFT computations. The reported enediyne metathesis paves the way to enantioselective enyne metathesis yielding chiral building blocks for compounds with potential biological activity, e.g. norsalvinorin or cacospongionolide B.

Keywords

enyne metathesis; enediyne; ring closing metathesis; ruthenium precatalyst; Diels-Alder reaction

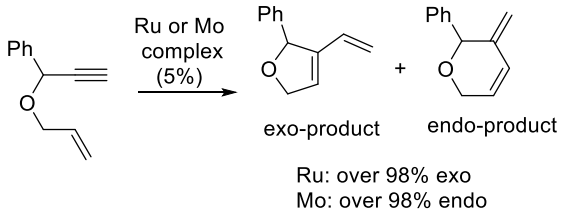
Introduction

Among the plethora of metathetic reactions of unsaturated compounds, e.g. alkene and enyne cross metathesis (CM [1] and EYCM [2-4]), alkene and enyne ring-closing metathesis (RCM and RCEYM) [5], ring-opening metathetic polymerization (ROMP) [6], etc., CM and RCM are most popular in organic synthesis. Furthermore, reactions of substrates containing three or more multiple bonds attracted special attention due to applications in tandem metathesis processes [7-8] or stereodiscriminating enantioselective ring-closing metathetic reactions [9-11].

In enantioselective RCM, prochiral trienes have been most often employed, leading to chiral cycloalkenes. Schrock molybdenum precatalysts [12-14] proved to be more effective than Grubbs or Collins ruthenium precatalysts [15-17] in the enantioselective RCM, however, their high air and moisture sensitivity makes their use less practical.

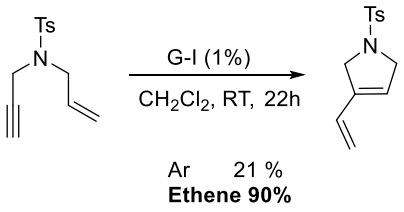
The choice of catalyst is one of the key elements in both cross and ring-closing enyne metathesis; the other is substrate structure. Both of these factors determine the metathesis mechanism: whether double (ene-then-yne mechanism) or triple (yne-then-ene mechanism) bond first enters the initiation step of the precatalyst activation.

Group 6 metal based precatalysts prefer the latter mechanism and yield *endo*-products, while Ru precatalysts allow both mechanisms and generally prefer the ene-then-yne mechanism for substrates with sterically unhindered double bond, yielding *exo*-products (Scheme 1) [18-21].



Scheme 1: RCEYM with Ru and Mo catalysts.

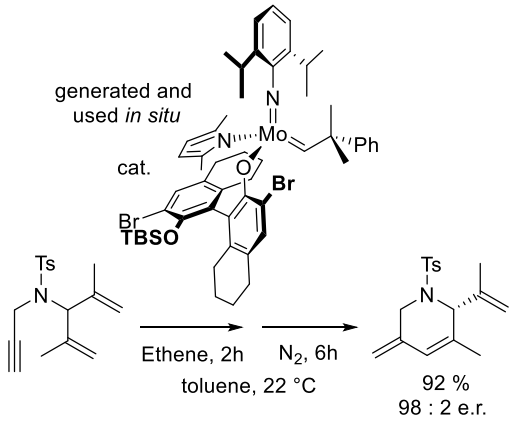
The presence of ethene (Mori conditions) is often benefitial in RCEYM, giving significantly better yields. This effect was explained to be caused not by improved activation of the ruthenium precatalyst, but either by participation in the second metathesis cycle releasing the diene product and returning methyleneruthenium complex to the catalytic cycle [19], or by preventing the catalytic intermediate to undergo subsequent metathesis reactions leading to catalyst deactivation [20]. In both cases, the effect of ethene was especially productive for the Grubbs 1st generation precatalyst and is typical for terminal alkynes or alkynes with little steric hindrance of the triple bond.



Scheme 2: Beneficial effect of ethene atmosphere.

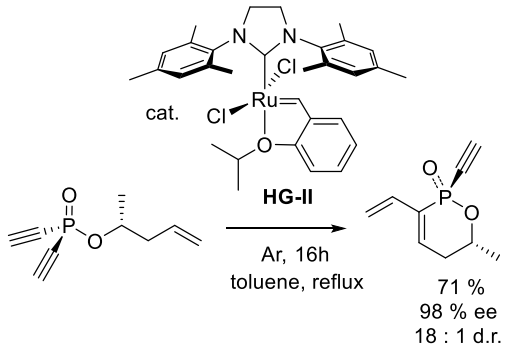
Despite the many examples of enantioselective RCM, only two examples of enantioselective RCEYM has been reported (both featuring a dienyne substrate and

a Schrock complex) [18,22]; no enantioselective enediyne metathesis or enantioselective RCEYM catalyzed by ruthenium complexes is known.



Scheme 3: Enantioselective dienyne metathesis [18].

The only RCEYM of the system containing two triple and one double bonds has been described by Gouverneour at al., who synthesized a series of dihydrooxaphosphinines by diastereoselective metathesis of alkenyl dialkynylphosphinates [23].



Scheme 4: Diastereoselective endiyne metathesis [23]

Thus, the possibility to perform desymmetrizing RCEYM of oxaenediynes, which should lead to chiral compounds bearing both alkyne and conjugated diene systems, seemed highly appealing to us. Before addressing enantioselective RCEYM, we report in this article scope and limitations of racemic metathesis with the emphasis on

catalysts used, optional application of Mori conditions and substitution in both alkyne and allyloxy part of the enediynes studied.

Results and Discussion

Choice and synthesis of starting substrates

In our research of desymmetrizing RCEYM of substrates bearing two triple and one double bonds, we decided to study prochiral oxaenediynes due to their potential synthetic availability. We originally considered three possible structures **1**-**3** (Fig. 1). However, in preliminary experiments, oxaenediyne **1** proved to be too unstable and prone to polymerization. On the other hand, the reactivity of oxaenediyne **3** was too sluggish. Hence, 4-(allyloxy)hepta-1,6-diyne (**2a**) and its derivatives became the framework of choice.

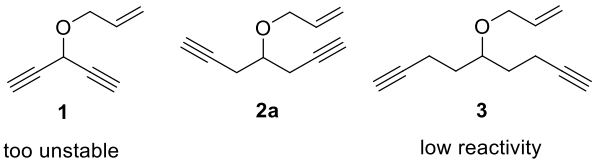
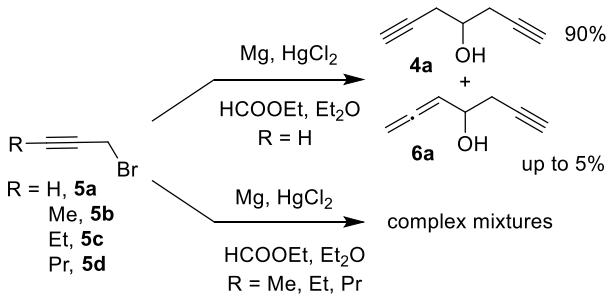


Figure 1: Oxaenediynes considered for the study of desymmetrizing RCEYM.

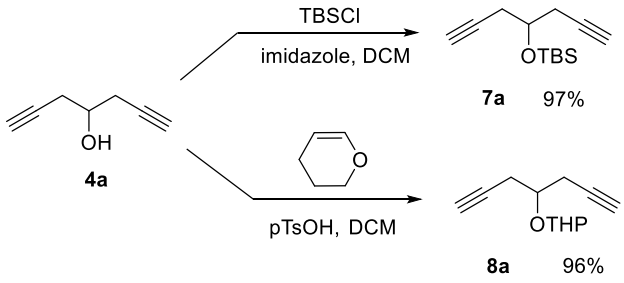
The key starting compound for the synthesis of oxaenediyne **2a** and its derivatives was hepta-1,6-diyn-4-ol (**4a**). It was prepared according to published procedure [24] by the reaction of ethyl formate with propargylmagnesium bromide, generated from propargyl bromide (**5a**), magnesium and catalytic amount of $HgCl_2$ to suppress the formation of allenylmagnesium bromide, with ethyl formate (Scheme 1). The target diynol **4a** was obtained in a 90% yield with up to 5% of hepta-1,2-dien-6-yn-4-ol (**6a**), which could not be directly separated from diynol **4a**, but its derivatives were later

conveniently removed by column chromatography in the subsequent steps. Unfortunately, analogous reactions of but-2-ynyl bromide (**5b**), pent-2-ynyl bromide (**5c**) and hex-2-ynyl bromide (**5d**) gave complex mixtures with significant admixtures of allenic products (Scheme 5).



Scheme 5: Synthesis of hepta-1,6-diyn-4-ol (**4a**).

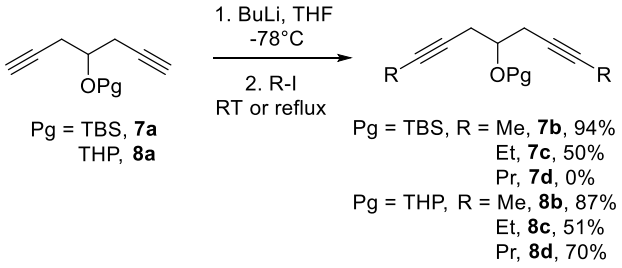
Alternative synthetic pathway to diynols **4b**-**4d** was hence developed consisting of protection of the hydroxyl group of diynol **4a** with *tert*-butyldiphenylsilyl according to Ref. [24] or with tetrahydropyranyl group. In both cases, we obtained the target products **7a**, **8a** in nearly quantitative yields. Interestingly, reaction time over 1 h in the THP protection led to formation of degradation products and significantly decreased yield (Scheme 6).



Scheme 6: Protection of hepta-1,6-diyn-4-ol (**4a**).

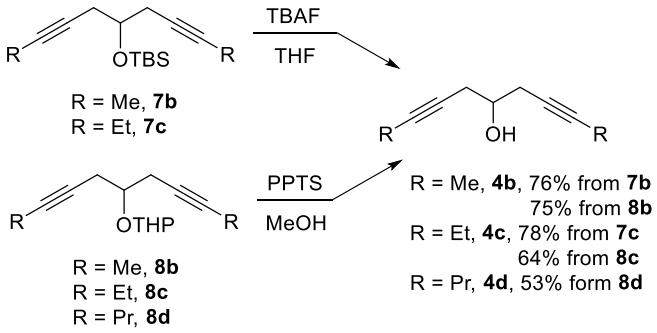
The TBS- or THP-protected alcohols **7a**, **8a** were alkylated in an analogy to the published procedure [25]. Thus, they were treated with an excess of BuLi (3.5-4

equiv) in THF at -78 °C, followed by addition of the respective alkyl iodides (4-5 equiv) and stirring the mixture either at RT (for R = Me) or at reflux (for R = Et, Pr). For longer alkyls, to achieve complete disubstitution was difficult and only moderate yields of products were obtained. Synthesis of oxadiynol **7d** failed. (Scheme 7).



Scheme 7: Alkylation of protected diynols **7a**, **8a**.

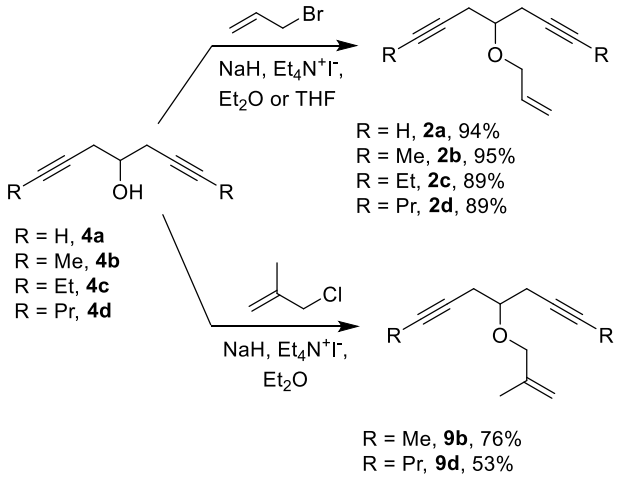
Alkylated diynols **7b**, **7c**, **8b**-**8d** were deprotected using standard methodologies in moderate to good yields (Scheme 8).



Scheme 8: Deprotection of protected diynols **7b**, **7c**, **8b**-**8d**.

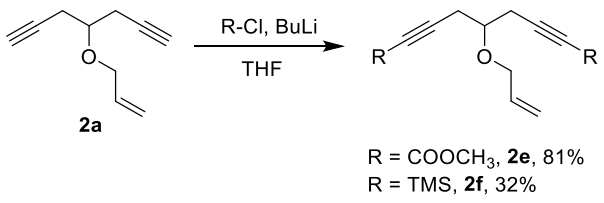
With diynols **4** in hand, we were able to synthesize a small library of allylated oxaenediynes **2** by alkylation of diynols **4** with allyl bromide, NaH and catalytic amount of tetraethylammonium iodide. Analogous synthesis of selected methallylated oxaenediynes **9** required longer reaction time and higher excess of methallyl chloride

(3 equiv). Unreacted diynols **4** could be recovered with advantage by column chromatography (Scheme 9).



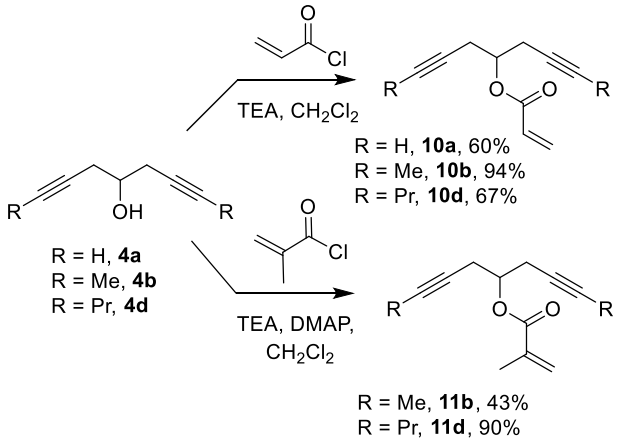
Scheme 9: Synthesis of oxaenediynes **2**, **9** bearing allyl or methallyl group.

With the aim to enable further functionalization of the products of oxaenediyne metathesis, we also synthesized substrates modified at the terminal alkyne positions with silyl or ester groups. Because these substrates are inaccessible by the above described methods, we obtained them by substituting terminal acetylenic hydrogens of parent oxaenediyne **2a** using butyllithium and methyl chloroformate or chlorotrimethylsilane (Scheme 10). Target disubstituted products **2e**, **2f** were formed in acceptable to good yields, complete disubstitution being again the issue.



Scheme 10: Synthesis of oxaenediynes **2e**, **2f** bearing ester or silyl groups.

To evaluate how electron density on the double bond of oxaenediyne could influence RCEYM, we also synthesized oxaenediynes bearing electron-deficient double bond from enediynols **4** and acryloyl chloride or methacryloyl chloride with triethylamine as a base. Formation of less reactive methacrylates **11** required longer reaction times and the use of DMAP as additive (Scheme 11).



Scheme 11: Synthesis of alkadiynyl acrylates **10** and methacrylates **11**

RCEYM of oxaenediynes **2**, **9-11**

As was mentioned in the Introduction, substrate structure [20-21,26-28] , the choice of precatalyst [21] and the presence of ethene (Mori conditions) [19-20,29] are major factors influencing the success of RCEYM. As precatalysts, we chose Grubbs 1st and 2nd generation (**G-I** and **G-II**), as well as more stable Hoveyda-Grubbs 2nd generation (**HG-II**) complexes (Fig. 2). Room temperature (25 °C) was chosen as it is common for this type of reactions.

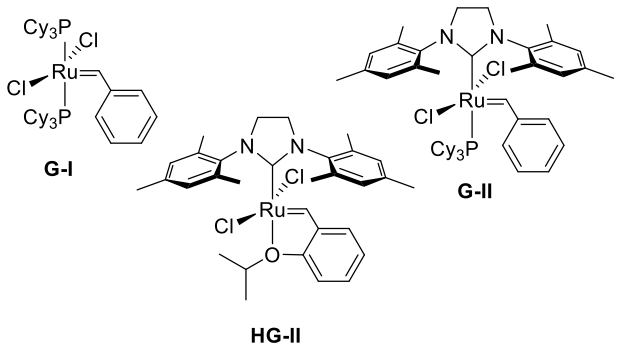
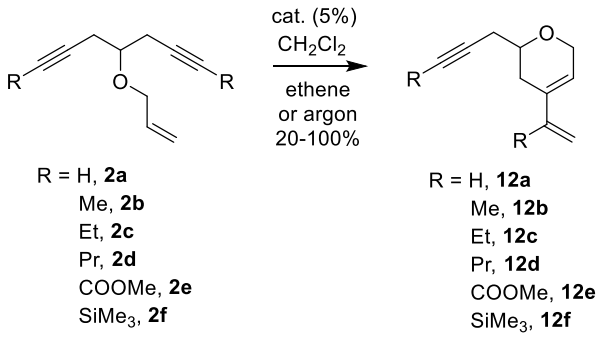


Figure 2: Ruthenium precatalysts employed.

We started our study with substrates **2**, bearing unsubstituted allyl chain (Scheme 12). The results of individual experiments and the role of substrate structure, precatalyst employed and atmosphere are listed in Table 1.



Scheme 12: RCEYM of oxaenediynes **2**

Table 1: RCEYM of oxaenediynes **2** (NMR yields).

Substrate	R	Product	Catalyst					
			G-I		**G-II**		**HG-II**	
			Atmosphere		Atmosphere		Atmosphere	
			Ethene	Argon	Ethene	Argon	Ethene	Argon
			Yield (%)		Yield (%)		Yield (%)	
2a	H	**12a**	92	100	35[a,b]	7	< 5[a,b]	< 5[b]
2b	Me	**12b**	100	78	28[a,b]	61	40[a,b]	64
2c	Et	**12c**	100	53	29[a,b]	66	27[a,b]	70
2d	Pr	**12d**	100	52	13[a,b]	98	67[a,b]	90

2e	CO_2Me	**12e**	100	100	18[a,b]	36	50[a,b]	78
2f	$SiMe_3$	**12f**	20[b]	0	< 5[a,b]	0.5	< 5[a,b]	11

[a] contains side-products from CM with ethene (Fig. 3). [b] the yield was estimated from the non-separable product mixture.

In the case of catalysis with **G-I**, ethene atmosphere strongly promoted the reaction, suppressing a number of unwanted processes as described in Refs. [19-20] and giving full or nearly full conversion with the exception of silylated oxaenediyne **2f** in an analogy to similar published substrates [29]. Quite surprisingly, the necessity of steric hindrance at propargylic position in RCEYM forming five-membered rings, as described in Ref. [20], was not observed in our cases. The absence of ethene resulted in a significant decrease of the yield, which gradually fell from R = H (**2a**) to R = Pr (**2d**). The reaction was not sensitive to the presence of electron-acceptor groups (R = COOMe, **2e**) at the triple bonds. Again, substrate **2f** containing bulkier electron-donor silyl groups gave only low yields of products. With the exception of silylated product **12f**, all substituted dihydropyrans **12a**-**12e** were isolated as pure racemic compounds in excellent yields when **G-I** precatalyst and ethene atmosphere were chosen.

In contrast to **G-I**, the presence of ethene atmosphere was highly detrimental for RCEYM catalyzed by more stable and active **G-II** and **HG-II** precatalysts, as it led to intermolecular cross-metathesis between the triple bonds and ethene in an analogy to previous observations (Figure 3) [21]. Thus, complex inseparable mixtures with not fully assignable ^{1}H NMR spectra were obtained in all cases.

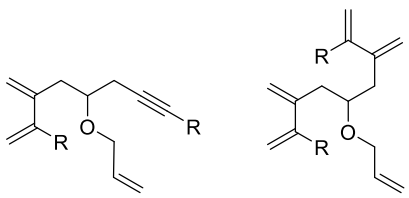


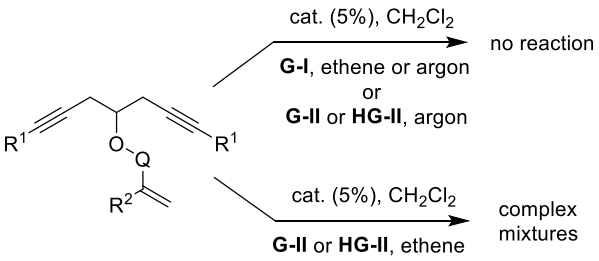
Figure 3: Examples of side products of CM with ethene.

The results of RCEYM in the absence of ethene were significantly better, although did not reach those using **G-I** catalyst and Mori conditions. The yields gradually improved with increasing steric hindrance of the triple bonds from oxaenediyne **2a** (R = H) to **2d** (R = Pr) for both precatalysts **G-II** and **HG-II**. This is in agreement with Ref [20], which proved that ruthenium-containing metathesis intermediate, formed by alkene cross metathesis in the initation step followed by RCEYM, can be deactivated by a subsequent reaction with the triple bond of the second enyne molecule. The results of RCEYM of ester-modified oxaenediyne **2e** were significantly better for more stable **HG-II** precatalyst, but still inferior to **G-I** catalysis. Again, very low yields were obtained for RCEYM of silylated oxaenediyne **2f**.

In a sharp contrast to relatively low sensitivity of oxaenediynes studied to the substitution of the triple bonds, modifications of the allyl group resulted in critical loss of reactivity. Thus, oxaenediynes **9** bearing methallyl group did not undergo RCEYM under **G-I** catalysis at all, regardless of the atmosphere (ethene or argon) chosen. Similarly, the use of more active catalysts **G-II** and **HG-II** under argon atmosphere failed to afford any products. On the other hand, catalysis with **HG-II** under Mori conditions (ethene atmosphere) gave only inseparable complex mixtures, in which products of cross metathesis with ethene prevailed and the target products could not be identified (Scheme 13).

To study the role of electron density of the double bond, we also attempted RCEYM of alkadiynyl acrylates **10** and alkadiynyl methacrylates **11**. Lower reactivity of the double bond in these substrates led to negative results analogous to methallyl group containing oxaenediynes **9**, i.e. no reaction for **G-I** catalysis and **G-II** or **HG-II**

catalysis under argon, or complex mixture formation for **G-II** or **HG-II** catalysis using Mori conditions (Scheme 10).

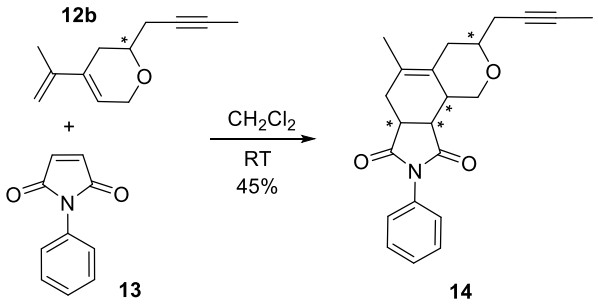


R^1 = Me, R^2 = Me, Q = CH_2, **9b**
R^1 = Pr, R^2 = Me, Q = CH_2, **9d**
R^1,R^2 = H, Q = CO, **10a**
R^1 = Me, R^2 = H, Q = CO, **10b**
R^1 = Pr, R^2 = H, Q = CO, **10d**
R^1,R^2 = Me, Q = CO, **11b**
R^1 = Pr, R^2 = Me, Q = CO, **11d**

Scheme 13: Attempted RCEYM of oxaenediynes **9**, alkadiynyl acrylates **10** and methacrylates **11**.

Diels-Alder reaction of RCEYM product **12b**

In general, RCEYM of enynes leads to products containing a conjugated double bond system, which can undergo Diels-Alder reaction and further can be employed in the synthesis of biologically active compounds, for example cacospongiolide B [30], norsalvinorin A [31] or salvinorin A [32]. Substituted dihydropyrans **12** obtained by RCEYM of oxaenediynes **2** contain both triple bond and conjugated diene systems. We were interested in their possible orthogonal transformations and hence carried out Diels-Alder reaction of dihydropyran **12b** with *N*-phenylmaleimide (**13**) in analogy to Ref. [33]. The reaction at RT in dichloromethane gave the target product **14** in a moderate 45% isolated yield as a mixture of two diastereoisomers (Scheme 14). Pure diastereoisomers were obtained by column chromatography in the yields 24% and 17%.



Scheme 14: Diels-Alder reaction of dihydropyran **12b** with *N*-phenylmaleimide (**13**).

DFT study of Diels-Alder reaction of compounds **12b** and **13**

Hexahydropyranoisoindole **14** contains four stereogenic centres and hence can form 8 possible diastereoisomers. Due to fixed configuration of maleimide **13**, four possible diastereoisomers come into account (Fig. 4).

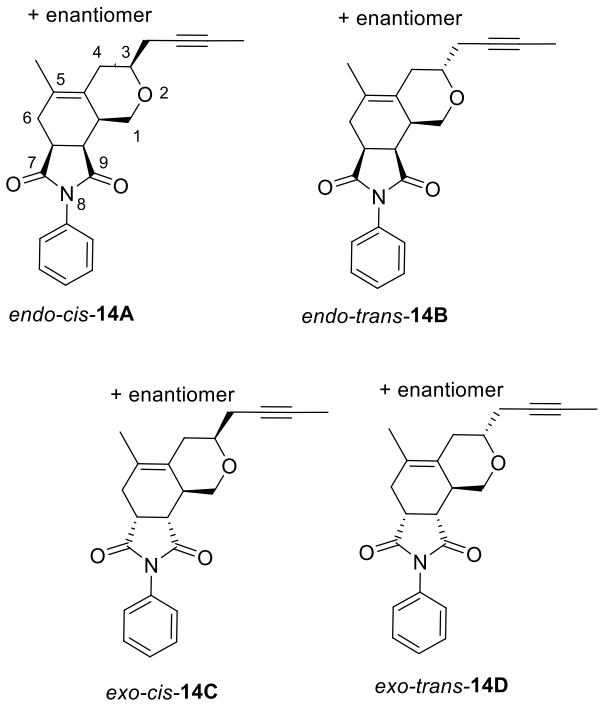


Figure 4. Four possible diastereoisomers of hexahydropyranoisoindole **14**

With the aim to disclose most probable candidates for experimentally obtained two diastereoisomers, we decided to perform a short DFT study of the Diels-Alder

reaction between dihydropyran **12b** and maleimide **13**. We started the study with optimization of the starting compound. While optimization of rigid maleimide **13** was straightforward, 18 conformations had to be considered for dihydropyran **12b**, namely all combinations of equatorial or axial position of the but-2-ynyl substituent, three staggered conformations of prop-1-ynyl with respect to the C-O bond of the ring, and three conformations of the dienyl system (*s-trans* and two tilted *s-cis* conformations) (Fig. 5).

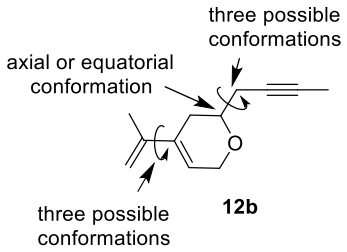


Figure 5. Conformations of **12b**

Among 18 conformations, the structure with equatorial conformation of but-2-ynyl group, *anti*-arrangement of O-C bond and prop-1-ynyl group, and *s-trans* conformation of the diene system proved to be most stable by more than 7 kJ/mol (Fig. 6). Of course, this conformation cannot enter Diels-Alder reaction and hence the more stable *s-cis* conformation with identical conformational arrangement of the other two parameters, although less stable by about 9 kJ/mol, was considered as the starting geometry for the Diels-Alder reaction (Fig. 6).

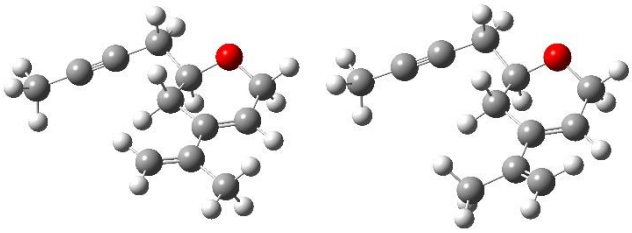
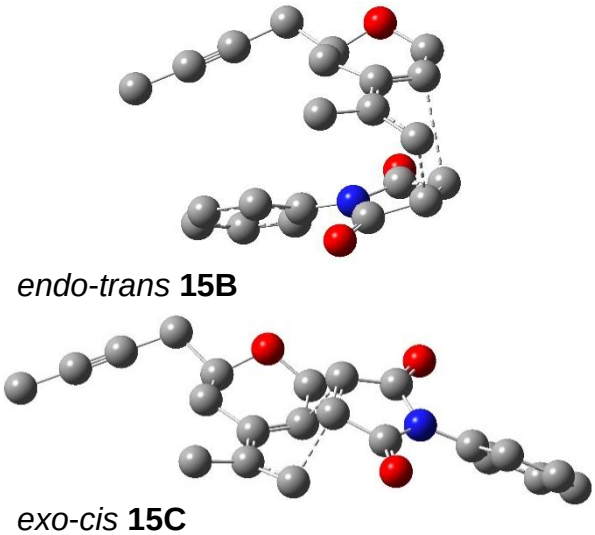


Figure 6. Most stable *s-trans* (left) and *s-cis* (right) conformations of dihydropyran **12b**

Search for the saddle points (starting complexes of both unsaturated compounds **12b** and **13**, transition states **15A**-**15D** and the corresponding Diels-Alder products **14A**-**14D** (Fig. 4)) showed that the reaction is strongly exergonic and irreversible with activation free Gibbs energy in the range between 46 and 76 kJ/mol. From the activation free Gibbs energies results that two main stereoisomers should be formed, namely *endo-trans* **14B** (99%) and *exo-cis* **14C** (1%). The difference among computed (99% and 1%) and experimentally observed values (29% and 16%) can be explained by participation of other conformations, lower accuracy of pure functional used and incompleteness of double zeta basis set. The structures of the corresponding transition states **15B**, **15C** are depicted in Fig. 7, relative free Gibbs energies of all saddle points for all four stereoisomers are shown in Fig. 8.



endo-trans **15B**

exo-cis **15C**

Figure 7. Two most stable transition states *endo-trans* **15B** and *exo-cis* **15C** (hydrogens are omitted for clarity).

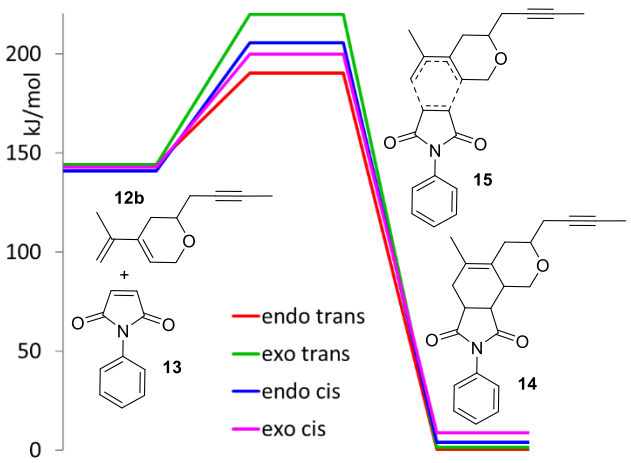


Figure 8. PES of Diels-Alder reaction of dihydropyran **12b** and maleimide **13**

Conclusions

In the study of ring-closing enyne metathesis of oxaenediynes, we found that the reaction is highly sensitive to the substitution in the allyloxy chain. While oxaenediynes bearing unsubstituted allyl chain gave moderate to excellent yields of the target substituted dihydropyrans bearing alkynyl and vinyl groups, substitution of allyl group for methallyl, acryloyl or methacryloyl resulted in complete loss of reactivity or formation of highly complex mixtures. On the other hand, the reaction showed significantly lower sensitivity to terminal modification of the triple bonds, tolerating well various alkyl or ester groups. Among the catalysts used, Grubbs 1st generation catalyst under Mori conditions worked best, while Grubbs and Hoveyda-Grubbs 2nd generation precatalysts gave lower yields. For 2nd generation precatalysts, Mori conditions could not be used due to multiple side metathesis reactions with ethene. To illustrate possible orthogonal modifications of the products bearing triple bond and conjugated diene system, we performed pilot Diels-Alder reaction with *N*-phenylmaleimide. Two main diastereomers were formed, the structures of which were estimated by DFT computations. Scope and limitations of oxaenediyne ring-

closing enyne metathesis disclosed here gave us essential information for continuing study on enantioselective variant of this reaction.

Experimental

General comments

Temperature data were uncorrected. NMR spectra were recorded with a Varian MercuryPlus spectrometer, ^{1}H NMR spectra at 299.97 MHz and ^{13}C NMR spectra at 75.77 MHz, or with a Agilent 400-MR DDR2 spectrometer, ^{1}H NMR spectra at 399.94 MHz and ^{13}C NMR spectra at 100.58 MHz, using residual deuterated solvent signals as the internal standards. Chemical shifts are given in parts per million, coupling constants in hertz. Mass spectra (ESI, APCI) and HRMS spectra were measure with a hybrid LTQ Obitrap XL instrument (Thermo Fisher Scientific). All reactions were performed in a dry inert atmosphere (Ar) in an oven-dried flasks. Anhydrous solvents were obtained from the PureSolv MD7 drying line (Innovation Technologies). *N*-Phenylmaleimide (**13**) was prepared according to Ref. [34].

Synthesis of starting oxaenediynes

Hepta-1,6-diyn-4-ol (4a) [24]

A mixture of Mg (6.69 g, 275 mmol) and $HgCl_2$ (122 mg, 449 mmol) in diethylether (130 ml) under inert atmosphere was cooled down to 0 °C. An 80 % solution of propargyl bromide in toluene (30 ml, 269 mmol) was added dropwise over 1h. The mixture was stirred at 0°C for 1h, then ethyl formate (7.5 ml, 8.18 g, 92.8 mmol) was added, the mixture was stirred for 2h at 0°C and then quenched with ice water (130 ml) and HCl (1.2 M solution, 260 ml). The organic layer was extracted with Et_2O (3 × 130 ml), the combined organic layers were washed with as saturated $NaHCO_3$ solution (30 ml) and dried over Na_2SO_4. Evaporation gave crude alcohol **4a**, which was distilled at reduced

pressure to give the desired hepta-1,6-diyn-4-ol (**4a**) as a clear oil (9.02 g, 90%, b.p. 88-91°C at 35 mbar). ^{1}H NMR: δ 2.09 (t, *J* = 2.7 Hz, 2H, C**H**≡C), 2.22 (d, *J* = 5.4 Hz, 1H, O**H**), 2.44-2.63 (m, 4H, C**H**$_2$), 3.97 (m, 1H, C**H**-CH$_2$).

4-(*Tert*-butyldimethylsilyloxy)hepta-1,6-diyne (7a) [24]

Tert-butyldimethylsilyl chloride (2.51 g, 16.7 mmol) and imidazole (1.14 g, 16.7 mmol) were added to hepta-1,6-diyn-4-ol (**4a**, 1.39 g, 12.8 mmol) in DCM (23 mL) at 0 °C. The reaction was allowed to warm to RT and stirred for 20h. After quenching with water (23 mL), extraction with DCM (3 × 23 mL) and drying over anh. MgSO$_4$, the solvent was evaporated and the crude product was purified by column chromatography (eluent hexane/EtOAc 40:1, Rf = 0.48) to give the desired silyl ether **7a** as a clear oil (2.86 g, quant.). ^{1}H NMR [24]: δ 0.12 (s, 6H, Si-C**H**$_3$), 0.91 (s, 9H, C**H**$_3$), 2.00 (t, *J* = 2.6 Hz, 2H, C**H**≡C), 2.44 (ddd, *J* = 16.7 Hz, *J* = 5.9 Hz, *J* = 2.6 Hz, 2H, C**H**$_2$), 2.51 (ddd, *J* = 16.7 Hz, *J* = 5.9 Hz, *J* = 2.6 Hz, 2H, C**H**$_2$), 3.97 (quint, *J* = 5.9 Hz, 1H, C**H**-CH$_2$).

2-(Hepta-1,6-diyn-4-yloxy)tetrahydro-*2H*-pyran (8a)

p-TsOH.H$_2$O (69 mg, 0.36 mmol) was added to hepta-1,6-diyn-4-ol (**4a**, 3.89 g, 36.0 mmol) in dichloromethane (57 mL) at 0 °C. 3,4-Dihydro-2*H*-pyran (3.33 g, 39.6 mmol) was slowly added, the mixture was stirred for 5 min at 0 °C and then for further 55 min at RT. The mixture was quenched with satd. NaHCO$_3$ solution (38 ml), the layers were separated and the water phase was extracted with dichloromethane (3 × 67 mL). The combined organic layers were dried over anh. MgSO$_4$, the solvent was carefully evaporated under reduced pressure and the crude product was purified by column chromatography (eluent hexane/EtOAc 32:1, Rf =0.21) to give the target

pyran **8a** as a clear oil (6.58 g, 96%). ^{1}H NMR: δ 1.50-1.91 (m, 6H, C**H**$_2$), 2.02 (dt, *J* = 8.8 Hz, *J* = 2.5 Hz, 2H, C≡C**H**), 2.53 (ddd, *J* = 17 Hz, *J* = 5.8 Hz, *J* = 2.7 Hz, 1H, C-C**H**$_2$), 2.57-2.69 (m, 3H, C-C**H**$_2$), 3.46-3.58 (m, 1H, O-C**H**$_2$), 3.90-4.01 (m, 2H, O-C**H**$_2$ + C**H**-CH$_2$), 4.82 (t, *J* = 3.5 Hz, 1H, O-C**H**-O). ^{13}C NMR: δ 19.2 (s, 1C, **C**H$_2$-CH$_2$), 22.9 (s, 1C, **C**H$_2$-C), 24.5 (s, 1C, **C**H$_2$-C), 25.3 (s, 1C, **C**H$_2$-CH$_2$), 30.5 (s, 1C, **C**H$_2$-CH$_2$), 62.3 (s, 1C, O-**C**H$_2$), 70.1 (s, 1C, **C**≡C), 70.3 (s, 1C, **C**≡CH), 72.9 (s, 1C, **C**H-O), 80.3 (s, 1C, C≡**C**H), 80.5 (s, 1C, C≡**C**H), 97.9 (s, 1C, O-**C**H-O). MS (EI$^+$), *m/z* (%): 153.1 [M-C$_3$H$_3$]$^+$ (30), 101.1 [C$_5$H$_9$O$_2$]$^+$ (40), 91.0 [C$_7$H$_7$]$^+$ (95), 85.7 [C$_6$H$_{13}$]$^+$ (100), 85.0 [C$_5$H$_9$O] (95), 67.0 [C$_5$H$_7$]$^+$ (88), 65.0 [C$_5$H$_5$]$^+$ (95), 56.1 [C$_3$H$_4$O]$^+$ (74). HRMS (EI$^+$): calcd. for C$_{12}$H$_{15}$O$_2$ ([M-H]$^+$) 191.1072, found 191.1077.

***Tert*-butyldimethyl(nona-2,7-diyn-5-yloxy)silane (7b)**

Butyllithium (6.0 mL, 14.4 mmol, 2.4 M solution in hexanes) was added dropwise at -78 °C to a solution of TBS ether **7a** (800 mg, 3.60 mmol) in dry THF (15 mL). The mixture was stirred at -78 °C for 1h, then methyl iodide (2.04 g, 14.4 mmol) was added, the mixture was allowed to warm to RT and stirred overnight. After quenching with saturated NH$_4$Cl solution (48 mL), the aqueous layer was extracted with diethyl ether (3 × 40 mL) and dried over anh. MgSO$_4$. Evaporation of solvents and subsequent column chromatography (eluent hexane/EtOAc 60:1, Rf = 0.38) gave TBS ether **7b** as a clear oil (850 mg, 94%). ^{1}H NMR: δ 0.11 (s, 6H, Si-C**H**$_3$), 0.91 (s, 9H, C**H**$_3$), 1.78 (t, *J* = 2.4 Hz, 6H, C≡C-C**H**$_3$), 2.31 (dm, *J* = 16.4 Hz, 2H, C**H**$_2$), 2.41 (dm, *J* = 16.4 Hz, 2H, C**H**$_2$), 3.86 (quint, *J* = 6.0 Hz, 1H, C**H**-CH$_2$). ^{13}C NMR: δ -4.7 (s, 2C, Si-**C**H$_3$), 3.5 (s, 2C, C≡C-**C**H$_3$), 18.2 (s, 1C, Si-**C**), 25.8 (s, 3C, Si-C-**C**H$_3$), 27.2 (s, 2C, **C**H$_2$), 71.0 (s, 1C, **C**H), 76.2 (s, 1C, **C**≡C-CH$_3$), 77.3 (s, 1C, C≡**C**-CH$_3$). MS (ESI$^+$), *m/z* (%): 273.1 [M+Na]$^+$ (40). HRMS (ESI): calcd. for C$_{15}$H$_{27}$OSi ([M+H]$^+$)

251.1826, found 251.1827. HRMS (ESI): calcd. for $C_{15}H_{26}ONaSi$ ($[M+Na]^+$) 273.1645, found 273.1645.

***Tert*-butyldimethyl(undeca-3,8-diyn-6-yloxy)silane (7c)**

Butyllithium (3.75 mL, 9.00 mmol, 2.4 M solution in hexanes) was added dropwise at -78 °C to a solution of TBS ether **7a** (667 mg, 3.00 mmol) in dry THF (13 mL). The mixture was stirred at -78 °C for 1h, then ethyl iodide (2.11 g, 13.5 mmol) was added, the mixture was allowed to warm to room temperature and then refluxed for 6h. After quenching with saturated NH_4Cl solution (25 mL), the aqueous layer was extracted with diethyl ether (3 × 25 mL) and dried over anh. $MgSO_4$. Evaporation of solvents and subsequent column chromatography (eluent hexane/CH_2Cl_2 7:1, Rf = 0.23) gave TBS ether **7c** as a clear oil (417 mg, 50%). ^{1}H NMR: δ 0.11 (s, 6H, Si-C**H**$_3$), 0.91 (s, 9H, C**H**$_3$), 1.12 (t, *J* = 7.5 Hz, 6H, CH_2-C**H**$_3$), 2.16 (qt, *J* = 7.5 Hz, *J* = 2.3 Hz, 4H, C**H**$_2$-CH_3), 2.33 (ddt, *J* = 16.3 Hz, *J* = 6.1 Hz, *J* = 2.3 Hz, 2H, CH-C**H**$_2$), 2.43 (ddt, *J* = 16.3 Hz, *J* = 6.1 Hz, *J* = 2.3 Hz, 2H, CH-C**H**$_2$), 3.85 (quint, *J* = 6.1 Hz, 1H, C**H**-CH_2). ^{13}C NMR: δ -4.6 (s, 2C, Si-**C**H$_3$), 12.5 (s, 2C, C**H**$_2$-CH_3), 14.2 (s, 2C, CH_2**C**H$_3$), 18.1 (s, 1C, Si-**C**), 25.8 (s, 3C, Si-C-**C**H$_3$), 27.3 (s, 2C, CH-**C**H$_2$), 71.0 (s, 1C, **C**H), 76.4 (s, 1C, **C**≡C-CH_2-CH_3), 83.3 (s, 1C, C≡**C**-CH_2-CH_3). MS (CI^+), *m/z* (%): 263.2 $[M-CH_3]^+$ (51), 221.1 $[M-C_4H_9]^+$ (100), 211.1 $[M-C_5H_7]^+$ (98), 147.1 $[M-C_6H_{15}OSi]^+$ (52), 73.0 $[C_4H_9O]^+$ (47). HRMS (CI^+): calcd. for $C_{17}H_{31}OSi$ ($[M+H]^+$) 279.2144, found 279.2140.

2-(Nona-2,7-diyn-5-yloxy)tetrahydro-2*H*-pyran (8b)

Butyllithium (27 mL, 60 mmol, 2.25 M solution in hexanes) was added dropwise at -78 °C to a solution of THP ether **8a** (2.88 g, 15.0 mmol) in dry THF (60 mL). The mixture was stirred at -78 °C for 1h, then methyl iodide (8.52 g, 60.0 mmol) was added, the mixture was allowed to warm to RT and stirred for 20h. After quenching

with saturated NH_4Cl solution (120 mL), the aqueous layer was extracted with diethyl ether (3 × 100 mL) and dried over anh. $MgSO_4$. Evaporation of solvents and subsequent column chromatography (eluent hexane/EtOAc 97:3, Rf = 0.22) gave THP ether **8b** as a clear oil (2.88 g, 87%). ^{1}H NMR: δ 1.47-1.90 (m, 12H, 3 × C**H**$_2$ + 2 × C**H**$_3$), 2.35-2.59 (m, 4H, C-C**H**$_2$), 3.46-3.56 (m, 1H, O-C**H**$_2$), 3.80-3.89 (m, 1H, C**H**-CH_2), 3.92-4.02 (m, 1H, O-C**H**$_2$), 4.82 (t, *J* = 3.5 Hz, 1H, O-C**H**-O). ^{13}C NMR: δ 3.49 (s, 1C, **C**H$_3$), 3.53 (s, 1C, **C**H$_3$), 19.4 (s, 1C, **C**H$_2$-CH_2), 23.2 (s, 1C, **C**H$_2$-C), 25.0 (s, 1C, **C**H$_2$-C), 25.4 (s, 1C, **C**H$_2$-CH_2), 30.7 (s, 1C, **C**H$_2$-CH_2), 62.2 (s, 1C, O-**C**H$_2$), 73.9 (s, 1C, CH_2-**C**H-O), 75.3 (s, 1C, **C**≡C), 75.5 (s, 1C, **C**≡C), 77.2 (s, 1C, C≡**C**), 77.3 (s, 1C, C≡**C**), 97.7 (s, 1C, O-**C**H-O). MS (CI$^+$), *m/z* (%): 119.1 [M-$C_5H_9O_2$]$^+$ (52), 85.1 [C_5H_9O]$^+$ (100), 83.0 [C_5H_7O]$^+$ (44). HRMS (CI$^+$): calcd. for $C_{14}H_{21}O_2$ ([M+H]$^+$) 221.1542, found 221.1540.

2-(Undeca-3,8-diyn-6-yloxy)tetrahydro-2*H*-pyran (8c)

Butyllithium (6.0 mL, 14.4 mmol, 2.4 M solution in hexanes) was added dropwise at -78 °C to a solution of THP ether **8a** (1.00 g, 5.20 mmol) in dry THF (20 mL). The mixture was stirred at -78 °C for 1h, then ethyl iodide (3.24 g, 20.8 mmol) was added, the mixture was allowed to warm to RT and then refluxed for 6h. After quenching with saturated NH_4Cl solution (48 mL), the aqueous layer was extracted with diethyl ether (3 × 40 mL) and dried over anh. $MgSO_4$. Evaporation of solvents and subsequent column chromatography (eluent hexane/EtOAc 25:1, Rf = 0.27) gave THP ether **8c** as a clear oil (660 mg, 51%). ^{1}H NMR: δ 1.12 (t, *J* = 7.5 Hz, 6H, C**H**$_3$), 1.48-1.91 (m, 6H, CH-C**H**$_2$-C**H**$_2$-C**H**$_2$), 2.11-2.21 (m, 4H, C**H**$_2$-CH_3), 2.42 (ddt, *J* = 16.6 Hz, *J* = 6.2 Hz, *J* = 2.5 Hz, 1H, C-C**H**$_2$-CH), 2.48-2.62 (m, 3H, C-C**H**$_2$-CH), 3.45-3.55 (m, 1H, O-C**H**$_2$), 3.86 (m, 1H, C**H**-CH_2), 3.92-4.05 (m, 1H, O-C**H**$_2$), 4.86 (t, *J* = 3.6 Hz, 1H, O-

C**H**-O). ^{13}C NMR: δ 12.4 (s, 1C, **C**H$_2$-CH$_3$), 12.5 (s, 1C, **C**H$_2$-CH$_3$), 14.2 (s, 1C, **C**H$_3$), 14.2 (s, 1C, **C**H$_3$), 19.4 (s, 1 C, **C**H$_2$-CH$_2$), 23.5 (s, 1C, C-**C**H$_2$-CH), 25.2 (s, 1C, C-**C**H$_2$-CH), 25.5 (s, 1C, **C**H$_2$-CH$_2$), 30.7 (s, 1C, **C**H$_2$-CH$_2$), 62.2 (s, 1C, O-**C**H$_2$), 74.1 (s, 1C, C-CH$_2$-**C**H), 75.7 (s, 1C, **C**≡C-CH$_2$-CH$_3$), 75.9 (s, 1C, **C**≡C-CH$_2$-CH$_3$), 83.3 (s, 1C, C≡**C**-CH$_2$-CH$_3$), 83.5 (s, 1C, C≡**C**-CH$_2$-CH$_3$), 97.8 (s, 1C, O-**C**H-O). MS (ESI$^+$), *m/z* (%): 272.2 [M+Na]$^+$ (100). HRMS (ESI$^+$): calcd. for $C_{16}H_{24}O_2Na$ ([M+Na]$^+$) 271.1669, found 271.1669.

2-(Trideca-4,9-diyn-7-yloxy)tetrahydro-2*H*-pyran (8d)

Butyllithium (16.8 mL, 42.0 mmol, 2.5 M solution in hexanes) was added dropwise at -78 °C to a solution of THP ether **8a** (2.31 g, 12.0 mmol) in dry THF (48 mL). The mixture was stirred at -78 °C for 1h, then propyl iodide (10.2 g, 60.0 mmol) was added, the mixture was allowed to warm to RT and then refluxed for 24h. After quenching with saturated NH_4Cl solution (90 mL), the aqueous layer was extracted with diethyl ether (3 × 75 mL) and dried over anh. $MgSO_4$. Filtration, careful evaporation of solvents and subsequent column chromatography (eluent hexane/EtOAc 30:1, Rf = 0.24) gave THP ether **8d** as a clear oil (2.31 g, 70%). ^{1}H NMR: δ 0.97 (t, *J* = 7.4 Hz, 6H, C**H**$_3$), 1.44-1.95 (m, 10H, C**H**$_2$-CH$_3$ + CH-C**H**$_2$-C**H**$_2$-C**H**$_2$), 2.08-2.18 (m, 4H, C**H**$_2$-CH$_2$-CH$_3$), 2.44 (ddt, *J* = 16.7 Hz, *J* = 6.2 Hz, *J* = 2.4 Hz, 1H, C-C**H**$_2$-CH), 2.49-2.62 (m, 3H, C-C**H**$_2$-CH), 3.46-3.56 (m, 1H, O-C**H**$_2$), 3.81-3.92 (m, 1H, C**H**-CH$_2$), 3.93-4.04 (m, 1H, O-C**H**$_2$), 4.86 (t, *J* = 3.5 Hz, 1H, O-C**H**-O). ^{13}C NMR: δ 13.5 (s, 1C, CH$_2$-**C**H$_3$), 13.5 (s, 1C, CH$_2$-**C**H$_3$), 19.4 (s, 1C, **C**H$_2$-CH$_2$), 20.8 (s, 1C, **C**H$_2$-CH$_2$-CH$_3$), 20.8 (s, 1C, **C**H$_2$-CH$_2$-CH$_3$), 22.4 (s, 1C, **C**H$_2$-CH$_3$), 22.4 (s, 1C, **C**H$_2$-CH$_3$), 23.4 (s, 1C, C-**C**H$_2$-CH), 25.2 (s, 1C, C-**C**H$_2$-CH), 25.5 (s, 1C, **C**H$_2$-CH$_2$), 30.7 (s, 1C, **C**H$_2$-CH$_2$), 62.2 (s, 1C, O-**C**H$_2$), 74.2 (s, 1C, C-CH$_2$-**C**H), 76.5 (s,

1C, **C**≡C-CH_2-CH_2), 77.2 (s, 1C, **C**≡C-CH_2-CH_2), 81.8 (s, 1C, C≡**C**-CH_2-CH_2), 81.9 (s, 1C, C≡**C**-CH_2-CH_2), 97.8 (s, 1C, O-**C**H-O). MS (ESI^+), *m/z* (%): 299.3 $[M+Na]^+$ (100). HRMS (ESI^+): calcd. for $C_{18}H_{28}O_2Na$ ($[M+Na]^+$) 299.1982, found 299.1982.

Nona-2,7-diyn-5-ol (4b)

From TBS ether **7b**: Tetrabutylammonium fluoride (1.18 g, 3.39 mmol, 75% soln. in water) in THF (5 mL) was added to TBS ether **7b** (850 mg, 3.39 mmol) in THF (8 mL) and the mixture was stirred for 46h. Evaporation of solvents and column chromatography (eluent hexane/EtOAc 20:3, Rf = 0.26) gave alcohol **4b** as a clear oil (351 mg, 76%).

From THP ether **8b**: A mixture of THP ether **8b** (2.87 g, 13.0 mmol) and pyridinium *p*-toluenesulfonate (327 mg, 1.30 mmol) in methanol (60 mL) was stirred for 3 days. Evaporation of solvents and column chromatography (eluent hexane/EtOAc 20:3, Rf = 0.26) gave alcohol **4b** as a clear oil (1.33 g, 75%). ^{1}H NMR: δ 1.81 (t, *J* = 2.4 Hz, 6H, C-C**H**$_3$), 2.35-2.54 (m, 4H, C**H**$_2$), 3.82 (quint, *J* = 5.9 Hz, 1H, C**H**-CH_2). ^{13}C NMR: δ 3.6 (s, 2C, **C**H_3), 26.4 (s, 2C, **C**H_2), 69.0 (s, 1C, **C**H), 74.7 (s, 2C, CH_2-**C**≡C), 78.6 (s, 2C, C≡**C**-CH_3). MS (ESI^+), *m/z* (%): 159.1 $[M+Na]^+$ (27). HRMS (ESI^+): calcd. for $C_9H_{12}ONa$ ($[M+Na]^+$) 159.0781, found 159.0782.

Undeca-3,8-diyn-6-ol (4c)

From TBS ether **7c**: Tetrabutylammonium fluoride (272 mg, 0.779 mmol, 75% soln. in water) in THF (2 mL) was added to TBS ether **7c** (217 mg, 0.779 mmol) in THF (1 mL) and the mixture was stirred for 5 days. Evaporation of solvents and column chromatography (eluent hexane/EtOAc 5:1, Rf = 0.48) gave alcohol **4c** as a clear oil (100 mg, 78%).

From THP ether **8c**: A mixture of THP ether **8c** (639 mg, 2.57 mmol) and pyridinium *p*-toluenesulfonate (65 mg, 0.26 mmol) in methanol (13 mL) was stirred for 4 days. Evaporation of solvents and column chromatography (eluent hexane/EtOAc 5:1, Rf = 0.48) gave alcohol **8c** as a clear oil (272 mg, 64%). ^{1}H NMR: δ 1.14 (t, *J* = 7.5 Hz, 6H, CH_2-C**H**$_3$), 2.19 (qt, *J* = 7.5 Hz, *J* = 2.4 Hz, 4H, C**H**$_2$-CH_3), 2.22-2.26 (bs, 1H, OH), 2.37-2.55 (m, 4H, CH-C**H**$_2$), 3.77-3.88 (m, 1H, C**H**-CH_2). ^{13}C NMR: δ 12.4 (s, 2C, **C**H_2-CH_3), 14.2 (s, 2C, **C**H_3), 26.4 (s, 2C, CH-**C**H_2), 69.0 (s, 1C, **C**H), 74.9 (s, 1C, **C**≡C-CH_2-CH_3), 84.7 (s, 1C, C≡**C**-CH_2-CH_3). MS (EI$^+$), *m/z* (%): 135.1 [M-C_2H_5]$^+$ (35), 97.1 [M-C_5H_7]$^+$ (37), 79.1 [M-C_5H_9O]$^+$ (37), 67.0 [M-C_6H_9O]$^+$(100), 53.0 [C_4H_5]$^+$(53). HRMS (EI$^+$): calcd. for $C_{11}H_{15}O$ ([M-H]$^+$) 163.1123, found 163.1125.

Trideca-4,9-diyn-7-ol (4d)

A mixture of THP ether **8d** (2.31 g, 8.35 mmol) and pyridinium *p*-toluenesulfonate (210 mg, 0.835 mmol) in methanol (41 mL) was stirred for 3 days. Evaporation of solvents and column chromatography (eluent hexane/EtOAc 7:1, Rf = 0.46) gave alcohol **4d** as a clear oil (851 mg, 53%). ^{1}H NMR: δ 0.98 (t, *J* = 7.4 Hz, 6H, CH_2-C**H**$_3$), 1.47-1.57 (m, 4H, C**H**$_2$-CH_3), 2.15 (tt, *J* = 7.0 Hz, *J* = 2.4 Hz, 4H, C**H**$_2$-CH_2-CH_3), 2.23 (d, *J* = 5.3 Hz, 1H, OH), 2.40-2.53 (m, 4H, CH-C**H**$_2$), 3.78-3.87 (m, 1H, C**H**-CH_2). ^{13}C NMR: δ 13.5 (s, 2C, CH_2-**C**H_3), 20.8 (s, 2C, **C**H_2-CH_2-CH_3), 22.4 (s, 2C, CH_2-**C**H_2-CH_3), 26.4 (s, 2C, CH-**C**H_2), 69.1 (s, 1C, **C**H), 75.7 (s, 1C, **C**≡C-CH_2-CH_2), 83.2(s, 1C, C≡**C**-CH_2-CH_2). MS (EI$^+$), *m/z* (%): 163.1 [M-C_2H_5]$^+$ (45), 145.1 [M-C_2H_7O]$^+$ (55), 93.1 [C_7H_9]$^+$ (57), 91.0 [C_7H_7]$^+$ (52), 79.1 [C_6H_7]$^+$ (51), 77.0 [C_6H_5]$^+$ (48), 67.0 [C_5H_7]$^+$(100), 53.0 [C_4H_5]$^+$(63). HRMS (EI$^+$): calcd. for $C_{13}H_{19}O$ ([M-H]$^+$) 191.1436, found 191.1432.

4-(Allyloxy)hepta-1,6-diyne (2a)

Sodium hydride (1.12 g, 60% in oil, 28.0 mmol) was added to a mixture of hepta1,6-diyn-4-ol (**4a**, 1.84 g, 16.0 mmol), allyl bromide (3.39 g, 28.0 mmol) and tetraethylammonium iodide (477 mg, 1.86 mmol) in dry THF (40 ml) at 0°C under argon atmosphere. The mixture was stirred at 0 °C for 10 min, then allowed to warm to RT and stirred for 2 days. After addition of satd. NH_4Cl solution (20 mL), the mixture was extracted with Et_2O (3 × 30 mL) and dried over anh. $MgSO_4$. Filtration and evaporation gave the crude product, which was purified by column chromatography (hexane/EtOAc 25:1, Rf = 0.5) to give 4-(allyloxy)hepta-1,6-diyne (**2a**) as a pale yellow oil (2.22 g, 94%). ^{1}H NMR: δ 2.00 (t, *J* = 2.7 Hz, 2H, C≡C**H**), 2.44-2.57 (m, 4H, CH-C**H**$_2$), 3.62 (quint, *J* = 5.7 Hz, 1H, C**H**), 4.07 (dm, *J* = 6.0 Hz, 2H, O-C**H**$_2$), 5.15 (d, *J* = 10.3 Hz, 1H, CH=C**H**$_2$), 5.27 (dm, *J* = 17.2 Hz, 1H, CH=C**H**$_2$), 5.83-5.94 (m, 1H, C**H**=CH$_2$). ^{13}C NMR: δ 23.2 (s, 2C, C-**C**H$_2$), 70.3 (s, 1C, O-**C**H$_2$), 70.5 (s, 2C, **C**≡C), 75.0 (s, 1C, **C**H-CH$_2$), 80.2 (s, 2C, C≡**C**H), 117.2 (s, 1C, CH=**C**H$_2$), 134.4 (s, 1C, **C**H=CH$_2$). MS (ESI$^-$), *m/z* (%): 147 [M-H]$^-$ (20), 127 [M-H$_2$-H$_2$O]$^-$ (26), 109 [M-C$_3$H$_3$]$^-$ (34), 89 [M-C$_3$H$_7$O]$^-$ (36), 87 [M-C$_3$H$_9$O]$^-$ (59), 75 [M-C$_4$H$_{10}$O]$^-$ (100), 67 [M-C$_5$H$_5$O]$^-$ (96). HRMS (ESI$^-$): calcd. for C$_{10}$H$_{11}$O ([M-H]$^-$) 147.0815, found 147.0812.

5-(Allyloxy)nona-2,7-diyne (2b)

Sodium hydride (131 mg, 60% in oil, 3.27 mmol) was added to a mixture of nona-2,7-diyn-5-ol (**4b**, 254 mg, 1.87 mmol), allyl bromide (396 g, 3.27 mmol) and tetraethyl-ammonium iodide (60 mg, 0.22 mmol) in dry Et_2O (20 mL) at 0 °C. The mixture was stirred at 0 °C for 10 min, then allowed to warm to RT and stirred for 3 days. After addition of saturated NH_4Cl solution (7 mL), the mixture was extracted with Et_2O (2 × 17 mL), washed with brine (17 mL) and dried over anh. $MgSO_4$. Filtration and

evaporation gave the crude product, which was purified by column chromatography (eluent hexane/EtOAc 50:1, Rf = 0.23) to give 5-(allyloxy)nona-2,7-diyne (**2b**) as a clear oil (314 mg, 95%). ^{1}H NMR: δ 1.78 (t, *J* = 2.5 Hz, 6H, C**H**$_3$), 2.37-2.56 (m, 4H, C-C**H**$_2$), 3.54 (quint, *J* = 5.7 Hz, 1H, C**H**), 4.09 (dt, *J* = 5.7 Hz, *J* = 1.4 Hz, 2H, C**H**$_2$), 5.17 (ddm, *J* = 10.4 Hz, *J* = 1.4 Hz, 1H, CH=C**H**$_2$), 5.29 (dm, *J* = 17.2 Hz, 1H, CH=C**H**$_2$), 5.85-6.00 (m, 1H, C**H**=CH$_2$). ^{13}C NMR: δ 3.6 (s, 2C, **C**H$_3$), 23.7 (s, 2C, C-**C**H$_2$), 70.6 (s, 1C, O-**C**H$_2$), 75.2 (s, 1C, **C**H), 76.2 (s, 1C, CH$_2$-**C**≡C), 77.5 (s, 1C, C≡**C**-CH$_3$), 117.1 (s, 1C, CH=**C**H$_2$), 134.9 (s, 1C, **C**H=CH$_2$). MS (ESI$^+$), *m/z* (%): 199.1 [M+Na]$^+$ (100). HRMS (ESI$^+$): calcd. for C$_{12}$H$_{17}$O ([M+H]$^+$) 177.1274, found 177.1275. HRMS (ESI$^+$): calcd. for C$_{12}$H$_{16}$ONa ([M+Na]$^+$) 199.1093, found 199.1094.

6-(Allyloxy)undeca-3,8-diyne (2c)

Sodium hydride (116 mg, 60% in oil, 2.90 mmol) was added to a mixture of undeca-3,8-diyn-6-ol (**4c**, 272 mg, 1.66 mmol), allyl bromide (351 mg, 2.90 mmol) and tetraethylammonium iodide (53 mg, 0.19 mmol) in dry THF (7 mL) at 0 °C. The mixture was stirred at 0°C for 10 min, then allowed to warm to RT and stirred for 4 days. After addition of saturated NH$_4$Cl solution (7 mL), the mixture was extracted with Et$_2$O (2 × 16 mL) and dried over anh. MgSO$_4$. Filtration and careful evaporation gave the crude product, which was purified by column chromatography (eluent hexane/EtOAc 50:1, Rf = 0.25) to give 6-(allyloxy)undeca-3,8-diyne (**2c**) as a clear oil (303 mg, 89%). ^{1}H NMR: δ 1.13 (t, *J* = 7.5 Hz, 6H, C**H**$_3$), 2.18 (qt, *J* = 7.5 Hz, *J* = 2.4 Hz, 4H, C**H**$_2$-CH$_3$), 2.38-2.57 (m, 4H, CH-C**H**$_2$), 3.56 (quint, *J* = 5.8 Hz, 1H, C**H**), 4.12 (dm, *J* = 5.6 Hz, 2H, O-C**H**$_2$), 5.18 (dm, *J* = 10.4 Hz,1H, CH=C**H**$_2$), 5.31 (dm, *J* = 17.2 Hz, 1H, CH=C**H**$_2$), 5.86-6.02 (m, 1H, C**H**=CH$_2$). ^{13}C NMR: δ 12.5 (s, 2C, **C**H$_2$-CH$_3$), 14.2 (s, 2C, **C**H$_3$), 23.9 (s, 2C, CH-**C**H$_2$), 70.7 (s, 1C, O-**C**H$_2$), 75.6 (s, 1C, **C**≡C-CH$_2$-

CH_3), 76.4 (s, 1C, **C**H), 83.5 (s, 1C, C≡**C**-CH_2-CH_3), 117.0 (s, 1C, CH=**C**H_2), 135.0 (s, 1C, **C**H=CH_2). MS (EI^+), *m/z* (%): 137.1 $[M\text{-}C_5H_7]^+$ (97), 95.0 $[C_7H_{11}]^+$ (72), 91.0 $[C_7H_7]^+$ (84), 79.0 $[C_6H_7]^+$ (85), 67.0 $[C_5H_7]^+$ (100), 57.0 $[C_3H_5O]^+$ (95). HRMS (EI^+): calcd. for $C_{14}H_{19}O$ ($[M\text{-}H]^+$) 203.1436, found 203.1432.

7-(Allyloxy)trideca-4,9-diyne (2d)

Sodium hydride (313 mg, 60% in oil, 7.83 mmol) was added to a mixture of trideca-4,9-diyn-7-ol (**4d**, 851 mg, 4.47 mmol), allyl bromide (947 mg, 7.83 mmol) and tetraethylammonium iodide (144 mg, 0.519 mmol) in dry Et_2O (19 mL) at 0 °C. The mixture was stirred at 0 °C for 10 min, then allowed to warm to RT and stirred for 2 days. After addition of saturated NH_4Cl solution (19 mL), the mixture was extracted with Et_2O (3 × 29 mL) and dried over anh. $MgSO_4$. Filtration and evaporation gave the crude product, which was purified by column chromatography (eluent hexane/EtOAc 50:1, Rf = 0.35) to give 7-(allyloxy)trideca-4,9-diyne (**2d**) as a clear oil (927 mg, 89%). ^{1}H NMR: δ 0.98 (t, *J* = 7.5 Hz, 6H, C**H**$_3$), 1.52 (m, 4H, C**H**$_2$-CH_3), 2.14 (tt, *J* = 7.0 Hz, *J* = 2.4 Hz, 4H, C**H**$_2$-CH_2-CH_3), 2.43-2.56 (m, 4H, CH-C**H**$_2$), 3.57 (quint, *J* = 5.8 Hz, 1H, C**H**), 4.12 (dt, *J* = 5.6 Hz, *J* =1.4 Hz, 2H, O-C**H**$_2$), 5.18 (dm, *J* = 10.4 Hz,1H, CH=C**H**$_2$), 5.31 (dm, *J* = 17.3 Hz, 1H, CH=C**H**$_2$), 5.88-5.99 (m, 1H, C**H**=CH_2). ^{13}C NMR: δ 13.5 (s, 2C, **C**H_3), 20.8 (s, 2C, **C**H_2-CH_2-CH_3), 22.4 (s, 2C, CH_2-**C**H_2-CH_3), 23.9 (s, 2C, CH-**C**H_2), 70.7 (s, 1C, O-**C**H_2), 76.4 (s, 1C, **C**≡C-CH_2-CH_2), 76.5 (s, 1C, **C**H), 82.0 (s, 1C, C≡**C**-CH_2-CH_2), 117.0 (s, 1C, CH=**C**H_2), 135.0 (s, 1C, **C**H=CH_2). MS (CI^+), *m/z* (%): 175.1 $[M\text{-}C_3H_5O]^+$ (23), 151.1 $[M\text{-}C_6H_9]^+$ (100), 133.1 $[M\text{-}C_6H_{11}O]^+$ (30), 81.1 $[C_6H_9]^+$ (31). HRMS (CI^+): calcd. for $C_{16}H_{25}O$ ($[M+H]^+$) 233.1905, found 233.1906.

5-[(2-Methylallyl)oxy]nona-2,7-diyne (9b)

Sodium hydride (105 mg, 60% in oil, 2.62 mmol) was added to a mixture of nona-2,7-diyn-5-ol (**4b**, 204 mg, 1.50 mmol), 2-methylprop-2-enyl chloride (407 mg, 4.49 mmol) and tetraethylammonium iodide (125 mg, 0.449 mmol) in dry Et_2O (6 mL) at 0 °C. The mixture was stirred at 0 °C for 10 min, then allowed to warm to RT and stirred for 5 days. After addition of saturated NH_4Cl solution (6 mL), the mixture was extracted with Et_2O (2 × 10 mL) and dried over anh. $MgSO_4$. Filtration, evaporation and separation by column chromatography (eluent hexane/EtOAc 50:1, Rf = 0.30) gave ether **9b** as a clear oil (217 mg, 76%). ^{1}H NMR: δ 1.77-1.81 (m, 9H, C**H**$_3$), 2.39-2.57 (m, 4H, CH-C**H**$_2$), 3.53 (quint, *J* = 5.7 Hz, 1H, C**H**), 4.00 (s, 2H, O-C**H**$_2$), 4.91 (s, 1H, CH=C**H**$_2$), 5.00 (s, 1H, CH=C**H**$_2$). ^{13}C NMR: δ 3.6 (s, 2C, C≡C-**C**H$_3$), 19.5 (s, 1C, CH_2=C-**C**H$_3$), 23.6 (s, 2C, CH-**C**H$_2$), 73.3 (s, 1C, O-**C**H$_2$), 75.3 (s, 1C, **C**≡C-CH$_3$), 75.9 (s, 1C, **C**H), 77.4 (s, 1C, C≡**C**-CH$_3$), 112.7 (s, 1C, C=**C**H$_2$), 142.3 (s, 1C, **C**=CH$_2$). MS (ESI$^+$), *m/z* (%): 213.1 [M+Na]$^+$ (100). HRMS (ESI$^+$): calcd. for $C_{13}H_{19}O$ ([M+H]$^+$) 191.1430, found 191.1429. HRMS (ESI$^+$): calcd. for $C_{13}H_{18}ONa$ ([M+Na]$^+$) 213.1250, found 213.1248.

7-[(2-Methylallyl)oxy]trideca-4,9-diyne (9d)

Sodium hydride (70 mg, 60% in oil, 1.8 mmol) was added to a mixture of trideca-4,9-diyn-7-ol (**4d**, 192 mg, 1.00 mmol), 2-methylprop-2-enyl chloride (272 mg, 3.00 mmol) and tetraethylammonium iodide (83 mg, 0.30 mmol) in dry Et_2O (4 mL) at 0 °C. The mixture was stirred at 0 °C for 10 min, then allowed to warm to RT and stirred for 7 days. After addition of saturated NH_4Cl solution (4 mL), the mixture was extracted with Et_2O (2 × 7 mL) and dried over anh. $MgSO_4$. Filtration, evaporation and separation by gradient column chromatography (eluent hexane/EtOAc 65:1→20:1, Rf = 0.32 for hexane/EtOAc 55:1) gave ether **9d** as a clear oil (131 mg, 53%). Starting

trideca-4,9-diyn-7-ol (73 mg, 38%) was partially recovered. ^{1}H NMR: δ 0.97 (t, *J* = 7.5 Hz, 6H, CH_2-C**H**$_3$), 1.44-1.57 (m, 4H, C**H**$_2$-CH_3), 2.14 (tt, *J* = 7.0 Hz, *J* = 2.3 Hz, 4H, C**H**$_2$-CH_2-CH_3), 2.41-2.58 (m, 4H, CH-C**H**$_2$), 3.55 (quint, *J* = 5.7 Hz, 1H, C**H**), 4.01 (s, 2H, O-C**H**$_2$), 4.88-4.91 (s, 1H, C=C**H**$_2$), 4.99-5.02 (s, 1H, C=C**H**$_2$). ^{13}C NMR: δ 13.5 (s, 2C, CH_2-**C**H$_3$), 19.5 (s, 1C, CH_2=C-**C**H$_3$), 20.8 (s, 2C, **C**H$_2$-CH_2-CH_3), 22.4 (s, 2C, CH_2-**C**H$_2$-CH_3), 23.8 (s, 2C, CH-**C**H$_2$), 73.4 (s, 1C, O-**C**H$_2$), 76.3 (s, 1C, **C**H), 76.4 (**C**≡C-CH_2-CH_2), 81.9 (s, 1C, **C**≡C-CH_2-CH_2), 112.5 (s, 1C, C=**C**H$_2$), 142.4 (s, 1C, **C**=CH_2). MS (EI$^+$), *m/z* (%): 165.1 [M-C_6H_9]$^+$ (100), 123.1 [$C_8H_{11}O$]$^+$ (57), 121.1 [C_8H_9O]$^+$ (90), 109.1 [C_7H_9O]$^+$ (68), 105.1 [C_7H_5O]$^+$ (74), 95.1 [C_6H_7O]$^+$ (75), 93.1 [C_7H_9]$^+$ (98), 91.0 [C_6H_3O]$^+$ (85), 81.0 [C_6H_9]$^+$ (65), 79.0 [C_6H_7]$^+$ (93), 77.0 [C_6H_5]$^+$ (67), 71.0 [C_4H_7O]$^+$ (85), 55.0 [C_3H_3O]$^+$ (95). HRMS (EI$^+$): calcd. for $C_{17}H_{26}O$ ([M]$^+$) 246.1984, found 246.1985.

Dimethyl 5-(allyloxy)nona-2,7-diynedioate (2e)

Butyllithium (3.4 mL, 7.7 mmol, 2.3 M solution in hexanes) was added dropwise at -78 °C to a solution of oxaenediyne **2a** (520 mg, 3.51 mmol) in dry THF (13 mL). The mixture was stirred at -78 °C for 1h, then methyl chloroformate (1.53 g, 16.1 mmol) was added and the mixture was allowed to warm to RT over 4h. After quenching with saturated NH_4Cl solution (13 mL), the aqueous layer was extracted with diethyl ether (3 × 13 mL) and dried over anh. $MgSO_4$. Filtration and evaporation of solvents and subsequent column chromatography (eluent hexane/Et_2O 3:1, Rf=0.26) gave diester **2e** as a clear oil (751 mg, 81%). ^{1}H NMR: δ 2.70 (d, *J* = 5.6 Hz, 4H, CH-C**H**$_2$), 3.73-3.83 (m, 7H, C**H**-O + C**H**$_3$), 4.11 (dm, *J* = 5.7 Hz, 2H, O-C**H**$_2$), 5.23 (dm, *J* = 10.2 Hz, 1H, CH=C**H**$_2$), 5.32 (dm, *J* = 17.4 Hz, 1H, CH=C**H**$_2$), 5.84-5.98 (m, 1H, C**H**=CH_2). ^{13}C NMR: δ 24.1 (s, 2C, CH-**C**H$_2$), 52.7 (s, 2C, **C**H$_3$), 71.1 (s, 1C,

O-**C**H_2), 73.9 (s, 1C, **C**H-O), 74.9 (s, 2C, **C**≡C-CO), 84.7 (s, 2C, C≡**C**-CO), 118.0 (s, 1C, CH=**C**H_2), 134.0 (s, 1C, **C**H=CH_2), 153.8 (s, 2C, **C**=O). MS (CI^+), *m/z* (%): 265.1 $[M+H]^+$ (38), 201.1 $[M-C_2H_7O_2]^+$ (47), 191.0 $[M-C_3H_5O_2]^+$ (45), 173.1 $[M-C_3H_7O_3]^+$ (85), 167.1 $[M-C_5H_5O_2]^+$ (100), 145.1 $[M-C_4H_7O_4]^+$ (65), 117.1 $[M-C_5H_7O_5]^+$ (46), 107.1 $[C_8H_{11}]^+$ (61), 79.1 $[C_6H_7]^+$ (64). HRMS (CI^+): calcd. for $C_{14}H_7O_5$ ($[M+H]^+$) 265.1076, found 265.1078.

[4-(Allyloxy)hepta-1,6-diyne-1,7-diyl]bis(trimethylsilane) (2f)

Butyllithium (2.7 mL, 6.1 mmol, 2.25 M solution in hexanes) was added dropwise at -78 °C to a solution of oxaenediyne **2a** (222 mg, 1.50 mmol) in dry THF (7 mL). The mixture was stirred at -78 °C for 1h, then trimethylsilyl chloride (660 mg, 6.08 mmol) was added, the mixture was allowed to warm to RT and then stirred for 26h. After quenching with saturated NH_4Cl solution (8 mL), the aqueous layer was extracted with diethyl ether (3 × 5 mL) and dried over anh. Na_2SO_4. Evaporation of solvents and subsequent column chromatography (eluent hexane/EtOAc 98:2, Rf = 0.34) gave silylated oxaenediyne **2f** as a clear oil (140 mg, 32%). ^{1}H NMR (299.97 MHz, $CDCl_3$): δ 0.16 (s, 18H, Si-C**H**$_3$), 2.46-2.61 (m, 4H, C**H**$_2$), 3.66 (quint, *J* = 6.0 Hz, 1H, C**H**), 4.16 (dm, *J* = 5.3 Hz, 2H, O-C**H**$_2$), 5.19 (d, *J* = 10.3 Hz, 1H, CH=C**H**$_2$), 5.32 (dm, *J* = 17.1 Hz, 1H, CH=C**H**$_2$), 5.87-6.01 (m, 1H, C**H**=CH_2). ^{13}C NMR (75.44 MHz, $CDCl_3$): δ 0.0 (s, 6C, Si-**C**H_3), 25.5 (s, 2C, **C**H_2-C≡C), 71.1 (s, 1C, O-**C**H_2), 75.9 (s, 1C, **C**H), 86.6 (s, 2C, C≡**C**-Si), 103.3 (s, 2C, **C**≡C-Si), 117.1 (s, 1C, CH=**C**H_2), 134.8 (s, 1C, **C**H=CH_2). MS (ESI^+), *m/z* (%): 315.2 $[M+Na]^+$ (21), 156.1 $[C_8H_{16}OSi]^+$ (81), 116.1 $[C_6H_{16}Si]^+$ (78), 105.1 $[C_7H_5O]^+$ (100). HRMS (ESI^+): calcd. for $C_{16}H_{28}ONaSi_2$ ($[M+Na]^+$) 315.1571, found 315.1567.

Hepta-1,6-diyn-4-yl acrylate (10a)

Freshly distilled acryloyl chloride (462 mg, 5.10 mmol) in CH_2Cl_2 was added dropwise to a solution of diynol **4a** (368 mg, 3.40 mmol) and triethylamine (688 mg, 6.80 mmol) in CH_2Cl_2 (10 mL). After stirring for 10 min at 0 °C, the mixture was allowed to warm to RT and stirred for 6h. The mixture was quenched with water (20 mL), extracted with CH_2Cl_2 (3 × 10 mL) and dried over anh. Na_2SO_4. Careful evaporation gave the crude product, which was purified by column chromatography (eluent hexane/EtOAc 95:5, Rf = 0.42) to give acrylate **10a** as a clear oil (329 mg, 60%). ^{1}H NMR: δ 2.04 (t, *J* = 2.7 Hz, 2H, C≡C**H**), 2.61-2.78 (m, 4H, C-C**H**$_2$), 5.12 (quint, *J* = 5.8 Hz, 1H, CH_2-C**H**), 5.89 (dd, *J* = 10.4 Hz, *J* = 1.4 Hz, 1H, CH=C**H**$_2$), 6.15 (dd, *J* = 17.3 Hz, *J* = 10.4 Hz, 1H, CH=C**H**$_2$), 6.47 (dd, *J* = 17.3 Hz, *J* = 1.4 Hz, 1H, **C**H=CH$_2$). ^{13}C NMR: δ 22.8 (s, 2C, CH-**C**H$_2$), 69.7 (s, 1C, **C**H-CH$_2$), 71.0 (s, 1C, **C**≡CH), 78.8 (s, 1C, C≡**C**H), 128.1 (s, 1C, **C**H=CH$_2$), 131.6 (s, 1C, CH=**C**H$_2$), 165.3 (s, 1C, **C**=O). MS (CI$^+$), *m/z* (%): 163.1 $[M+H]^+$ (50), 123.0 $[M-C_3H_3]^+$ (100), 91.1 $[M-C_3H_3O_2]^+$ (80). HRMS (CI$^+$): calcd. for $C_{10}H_{11}O_2$ ($[M+H]^+$) 163.0759, found 163.0757.

Nona-2,7-diyn-5-yl acrylate (10b)

Nona-2,7-diyn-5-ol (**4b**, 250 mg, 1.84 mmol) and triethylamine (372 mg, 3.68 mmol) were dissolved in dry CH_2Cl_2 (6 mL) and the mixture was cooled down to 0 °C. Freshly distilled acryloyl chloride (250 mg, 2.76 mmol) was added dropwise and the mixture was stirred for 1h at 0 °C. After quenching with brine (4 mL), the layers were separated, the aqueous phase was extracted with Et_2O (2 × 6 mL) and the combined organic layers were dried over anh. Na_2SO_4. Careful evaporation gave the crude product, which was purified by column chromatography (eluent hexan/EtOAc 97:3, Rf = 0.32) to give acrylate **10b** as a clear oil (328 mg, 94%). ^{1}H NMR: δ 1.79 (t, *J* = 2.5 Hz, 6H, C**H**$_3$), 2.50-2.68 (m, 4H, C-C**H**$_2$), 5.01 (quint, *J* = 6.0 Hz, 1H, CH_2-C**H**), 5.85

(dd, *J* = 10.0 Hz, *J* = 1.4 Hz, 1H, CH=C**H**$_2$), 6.15 (dd, *J* = 17.5 Hz, *J* = 10.4 Hz, 1H, C**H**=CH$_2$), 6.45 (dd, *J* = 17.3 Hz, *J* = 1.4 Hz, 1H, CH=C**H**$_2$). ^{13}C NMR: δ 3.5 (s, 2C, **C**H$_3$), 23.2 (s, 2C, CH-**C**H$_2$), 71.0 (s, 1C, **C**H-CH$_2$), 73.4 (s, 1C, **C**≡C-CH$_3$), 78.1 (s, 1C, C≡**C**-CH$_3$), 128.5 (s, 1C, **C**H=CH$_2$), 131.0 (s, 1C, CH=**C**H$_2$), 165.4 (s, 1C, **C**=O). MS (ESI$^+$), *m/z* (%): 213.1 [M+Na]$^+$ (100). HRMS (ESI$^+$): calcd. for $C_{12}H_{15}O_2$ ([M+H]$^+$) 191.1067, found 191.1065. HRMS (ESI$^+$): calcd. for $C_{12}H_{14}O_2Na$ ([M+Na]$^+$) 213.0886, found 213.0885.

Trideca-4,9-diyn-7-yl acrylate (10d)

Trideca-4,9-diyn-7-ol (**4d**, 192 mg, 1.00 mmol) and triethylamine (202 mg, 2.00 mmol) were dissolved in dry CH_2Cl_2 (3.5 mL) and the mixture was cooled down to 0 °C. Freshly distilled acryloyl chloride (136 mg, 1.50 mmol) was added dropwise and the mixture was stirred for 90 min at 0 °C. After quenching with brine (2.5 mL), the layers were separated, the aqueous phase was extracted with Et_2O (2 × 3.5 mL) and the combined organic layers were dried over Na_2SO_4. Careful evaporation gave the crude product, which was purified by column chromatography (eluent hexan/EtOAc 55:1, Rf = 0.24) to give acrylate **10d** as a clear oil (166 mg, 67%). ^{1}H NMR: δ 0.97 (t, *J* = 7.4 Hz, 6H, C**H**$_3$), 1.44-1.56 (m, 4H, C**H**$_2$-CH$_3$), 2.13 (tt, *J* = 7.0 Hz, *J* = 2.3 Hz, 4H, C**H**$_2$-CH$_2$-CH$_3$), 2.53-2.69 (m, 4H, CH-C**H**$_2$), 5.04 (quint, *J* = 5.9 Hz, 1H, C**H**-CH$_2$), 5.85 (dd, *J* = 10.5 Hz, *J* = 1.4 Hz, 1H, CH=C**H**$_2$), 6.15 (dd, *J* = 17.0 Hz, *J* = 10.5 Hz, 1H, C**H**=CH$_2$), 6.44 (dd, *J* = 17.0 Hz, *J* = 1.4 Hz, 1H, CH=C**H**$_2$). ^{13}C NMR: δ 13.4 (s, 2C, **C**H$_3$), 20.7 (s, 2C, **C**H$_2$-CH$_2$-CH$_3$), 22.3 (s, 2C, CH$_2$-**C**H$_2$-CH$_3$), 23.3 (s, 2C, CH-**C**H$_2$), 71.0 (s, 1C, **C**H-CH$_2$), 74.9 (s, 1C, **C**≡C-CH$_2$-CH$_2$), 82.6 (s, 1C, C≡**C**-CH$_2$-CH$_2$), 128.5 (s, 1C, **C**H=CH$_2$), 130.9 (s, 1C, CH=**C**H$_2$), 165.4 (s, 1C, **C**=O). MS (EI$^+$), *m/z* (%): 145.1 [M-$C_5H_9O_2$]$^+$ (96), 131.1 [M-$C_6H_{11}O_2$]$^+$ (58), 117.1 [M-$C_7H_{13}O_2$]$^+$ (80), 91.0

$[C_7H_7]^+$ (48), 55.0 $[C_3H_3O]^+$ (100). HRMS (EI^+): calcd. for $C_{16}H_{22}O_2$ ($[M]^+$) 246.1620, found 246.1622.

Nona-2,7-diyn-5-yl methacrylate (11b)

Triethylamine (559 mg, 5.52 mmol) and 4-(dimethylamino)pyridine (34 mg, 0.28 mmol) were slowly added to a solution of nona-2,7-diyn-5-ol (**4b**, 250 mg, 1.84 mmol) in dry CH_2Cl_2 (5 ml) at 0 °C. Methacryloyl chloride (385 mg, 3.68 mmol) was added dropwise and the mixture was allowed to warm to RT and stirred for 24h. After quenching with saturated NH_4Cl (5 mL), the layers were separated, the aqueous phase was extracted with Et_2O (2 × 5 mL) and the combined organic layers were dried over anh. $MgSO_4$. Evaporation and purification by column chromatography (eluent hexan/EtOAc 97:3, Rf = 0.43) gave methacrylate **11b** as a clear oil (161 mg, 43%). ^{1}H NMR: δ 1.78 (t, *J* = 2.6 Hz, 6H, C≡C-C**H**$_3$), 1.96 (s, 3H, C**H**$_3$), 2.49-2.67 (m, 4H, C-C**H**$_2$), 4.97 (quint, *J* = 5.9 Hz, 1H, CH_2-C**H**), 5.57-5.60 (m, 1H, C=C**H**$_2$), 6.14-6.16 (m, 1H, C=C**H**$_2$). ^{13}C NMR: δ 3.2 (s, 2C, C≡C-**C**H_3), 17.9 (s, 1C, **C**H_3), 22.8 (s, 2C, C-**C**H_2), 70.8 (s, 1C, **C**H), 73.6 (s, 1C, **C**≡C-CH_3), 77.6 (s, 1C, C≡**C**-CH_3), 125.4 (s, 1C, C=**C**H_2), 136.0 (s, 1C, **C**=CH_2), 166.3 (s, 1C, **C**=O). MS (ESI^+), *m/z* (%): 227.1 $[M+Na]^+$ (100). HRMS (ESI^+): calcd. for $C_{13}H_{17}O_2$ ($[M+H]^+$) 205.1223, found 205.1224. HRMS (ESI^+): calcd. for $C_{13}H_{16}O_2Na$ ($[M+Na]^+$) 227.1043, found 227.1044.

Trideca-4,9-diyn-7-yl methacrylate (11d)

Triethylamine (405 mg, 4.00 mmol) and 4-(dimethylamino)pyridine (24 mg, 0.20 mmol) were slowly added to a solution of trideca-4,9-diyn-7-ol (**4d**, 192 mg, 1.00 mmol) in dry CH_2Cl_2 (3 mL) at 0 °C. Methacryloyl chloride (209 mg, 2.00 mmol) was added dropwise and the mixture was allowed to warm to RT and stirred for 20h. After quenching with saturated NH_4Cl (3 mL), the layers were separated, the aqueous

phase was extracted with Et_2O (2 × 3 mL) and the combined organic layers were dried over anh. $MgSO_4$. Careful evaporation and purification by column chromatography (eluent hexan/EtOAc 55:1, Rf = 0.23) gave methacrylate **11d** as a clear oil (234 mg, 90%). ^{1}H NMR: δ 0.96 (t, *J* = 7.3 Hz, 6H, CH_2-C**H**$_3$), 1.43-1.56 (m, 4H, C**H**$_2$-CH_3), 1.96 (s, 3H, C**H**$_3$), 2.12 (tt, *J* = 7.0 Hz, *J* = 2.3 Hz, 4H, C**H**$_2$-CH_2-CH_3), 2.53-2.69 (m, 4H, CH-C**H**$_2$), 5.01 (quint, *J* = 5.6 Hz, 1H, CH_2-C**H**), 5.56-5.59 (m, 1H, C=C**H**$_2$), 6.15 (s, 1H, C=C**H**$_2$). ^{13}C NMR: δ 13.4 (s, 2C, CH_2-**C**H_3), 18.2 (s, 1C, **C**H_3), 20.7 (s, 2C, **C**H_2-CH_2-CH_3), 22.3 (s, 2C, CH_2-**C**H_2-CH_3), 23.4 (s, 2C, CH-**C**H_2), 71.1 (s, 1C, **C**H-CH_2), 75.0 (s, 2C, **C**≡C-CH_2-CH_2), 82.5 (s, 2C, C≡**C**-CH_2-CH_2), 125.6 (s, 1C, C=**C**H_2), 136.3 (s, 1C, **C**=CH_2), 166.6 (s, 1C, **C**=O). MS (EI$^+$), *m/z* (%): 174.1 [M-M-$C_4H_6O_2$]$^+$ (62), 159.1 [M-$C_5H_9O_2$]$^+$ (55), 145.1 [M-$C_6H_{11}O_2$]$^+$ (100), 131.1 [M-$C_7H_{13}O_2$]$^+$ (80), 117.1 [M-$C_8H_{15}O_2$]$^+$ (95), 91.0 [C_7H_7]$^+$ (70). HRMS (EI$^+$): calcd. for $C_{17}H_{24}O_2$ ([M]$^+$) 260.1776, found 260.1775.

RCEYM of oxaenediynes

General procedure under ethene atmosphere (A)

Anhydrous dichloromethane was degassed and then percolated with ethene for several min. To oxaenediyne (1 equiv) in CH_2Cl_2 was added Grubbs or Hoveyda-Grubbs catalyst (0.05 equiv) in CH_2Cl_2 and the mixture was stirred under ethene atmosphere at 25 °C for 24h. Afterwards, the mixture was filtered through a short pad of silica, the silica was washed with CH_2Cl_2 and the organic solution was carefully evaporated to give the crude product. If necessary, products were purified by column chromatography.

General procedure under argon atmosphere (B)

Anhydrous dichloromethane was degassed before reaction. To oxaenediyne (1 equiv) in CH_2Cl_2 was added Grubbs or Hoveyda-Grubbs catalyst (0.05 equiv) in CH_2Cl_2 and the mixture was stirred under argon atmosphere at 25°C for 24h. Afterwards, the mixture was filtered through a short pad of silica, the silica was washed with CH_2Cl_2 and the organic solution was carefully evaporated to give the crude product. If necessary, products were purified by column chromatography.

4-Ethenyl-(2-prop-2-yn-1-yl)-3,6-dihydro-*2H*-pyran (12a)

According to General procedure A, from oxaenediyne **2a** (243 mg, 1.64 mmol) in CH_2Cl_2 (6 mL) using **G-I** (67.5 mg, 82.0 μmol) in CH_2Cl_2 (7 mL) as a catalyst, crude product was obtained which was further purified by column chromatography (eluent hexane/EtOAc 95:5, Rf = 0.54) to give dihydropyran **12a** as a clear oil (182 mg, 75%). ^{1}H NMR: δ 2.06 (t, *J* = 2.8 Hz, 1H, C**H**≡C), 2.13-2.23 (m, 1H, C**H**$_2$-C=CH), 2.34 (dt, *J* = 16.7 Hz, *J* = 2.8 Hz, 1H, C**H**$_2$), 2.49 (ddd, *J* = 16.7 Hz, *J* = 6.3 Hz, *J* = 2.8 Hz, 1H, C≡C-C**H**$_2$), 2.56 (ddd, *J* = 16.7 Hz, *J* = 5.6 Hz, *J* = 2.8 Hz, 1H, C≡C-C**H**$_2$), 3.65-3.76 (m, 1H, C**H**-O), 4.26-4.39 (m, 2H, O-C**H**$_2$), 5.02 (d, *J* = 10.7 Hz, 1H, CH=C**H**$_2$), 5.17 (d, *J* = 17.4 Hz, 1H, CH=C**H**$_2$), 5.73 (m, 1H, C=C**H**), 6.38 (dd, *J* = 17.4 Hz, *J* = 10.7 Hz, 1H, C**H**=CH$_2$). ^{13}C NMR: δ 25.5 (s, 1C, **C**H$_2$-C≡C), 28.9 (s, 1C, **C**H$_2$-C=CH), 66.0 (s, 1C, O-**C**H$_2$), 70.1 (s, 1C, H**C**≡C), 71.7 (s, 1C, **C**H-O), 80.5 (s, 1C, HC≡**C**), 111.6 (s, 1C, CH=**C**H$_2$), 126.0 (s, 1C, C=**C**H), 133.2 (s, 1C, **C**=CH), 137.9 (s, 1C, **C**H=CH$_2$). MS (CI$^+$), *m/z* (%): 149.1 [M+H]$^+$ (10), 109.1 [M-C_3H_3]$^+$ (100), 91.1 [C_7H_7]$^+$ (45), 81.1 [C_5H_5O]$^+$ (50). HRMS (CI$^+$): calcd. for $C_{10}H_{13}O$ ([M+H]$^+$) 149.0966, found 149.0964.

2-(But-2-yn-1-yl)-4-(prop-1-en-2-yl)-3,6-dihydro-2*H*-pyran (12b)

According to General procedure A, from oxaenediyne **2b** (130 mg, 0.738 mmol) in CH_2Cl_2 (6 mL) using **G-I** (6.1 mg, 0.0074 mmol) in CH_2Cl_2 (3 mL) as a catalyst, crude product was obtained which was further purified by column chromatography (eluent hexane/EtOAc 95:5, Rf = 0.41) to give dihydropyran **12b** as a clear oil (127 mg, 98%). ^{1}H NMR: δ 1.80 (t, *J* = 2.6 Hz, 3H, C≡C-C**H**$_3$), 1.90 (s, 3H, C-C**H**$_3$), 2.13-2.28 (m, 1H, C**H**$_2$-C=CH), 2.33 (dm, *J* = 16.4 Hz, 1H, C**H**$_2$-C=CH), 2.39-2.54 (m, 2H, C**H**$_2$-C≡C), 3.56-3.66 (m, 1H, C**H**-O), 4.25-4.43 (m, 2H, O-C**H**$_2$), 4.92 (s, 1H, C=C**H**$_2$), 5.01 (s, 1H, C=C**H**$_2$), 5.77-5.83 (m, 1H, C=C**H**). ^{13}C NMR: δ 3.6 (s, 1C, C≡C-**C**H$_3$), 20.2 (s, 1C, C-**C**H$_3$), 25.9 (s, 1C, **C**H$_2$-C≡C), 30.4 (s, 1C, **C**H$_2$-C=CH), 66.3 (s, 1C, O-**C**H$_2$), 72.5 (s, 1C, **C**H-O), 75.1 (s, 1C, C≡**C**-CH$_2$), 77.4 (s, 1C, CH$_3$-**C**≡C), 110.8 (s, 1C, C=**C**H$_2$), 122.0 (s, 1C, C=**C**H), 134.1 (s, 1C, **C**=CH), 142.0 (s, 1C, **C**=CH$_2$). MS (EI$^+$), *m/z* (%): 176 [M]$^+$ (5), 147 [M - CH$_2$=O + H$^+$]$^+$ (95), 121.1 [M - CH$_2$=O - CH≡CH + H$^+$]$^+$ (100). HRMS (EI$^+$): calcd. for $C_{12}H_{16}O$ ([M]$^+$) 176.1201, found 176.1208.

4-(But-1-en-2-yl)-2-(pent-2-yn-1-yl)-3,6-dihydro-2*H*-pyran (12c)

According to General procedure A, from oxaenediyne **2c** (31 mg, 0.15 mmol) in CH_2Cl_2 (1.2 mL) using **G-I** (6.2 mg, 7.6 μmol) in CH_2Cl_2 (1.2 mL) as a catalyst, dihydropyran **12c** of sufficient purity was obtained as a clear oil (27 mg, 87%). ^{1}H NMR: δ 1.09 (t, *J* = 7.3 Hz, 3H, C**H**$_3$-CH$_2$-C=CH$_2$), 1.13 (t, *J* = 7.5 Hz, 3H, C**H**$_3$-CH$_2$-C≡C), 2.19 (qt, *J* = 7.4 Hz, *J* = 2.4 Hz, 2H, CH$_3$-C**H**$_2$-C≡C), 2.21-2.39 (m, 4H, C**H**$_2$-C=CH + C**H**$_2$-C=CH$_2$), 2.43 (ddt, *J* = 16.6 Hz, *J* = 6.6 Hz, *J* = 2.4 Hz, 1H, C≡C-C**H**$_2$-CH), 2.51 (ddt, *J* = 16.6 Hz, *J* = 5.5 Hz, *J* = 2.4 Hz, 1H, C≡C-C**H**$_2$-CH), 3.59-3.67 (m, 1H, CH-O), 4.27-4.40 (m, 2H, O-C**H**$_2$), 4.92 (s, 1H, C=C**H**$_2$), 5.03 (s, 1H, C=C**H**$_2$), 5.81-5.84 (m, 1H, C=C**H**). ^{13}C NMR: δ 12.4 (s, 1C, CH$_3$-**C**H$_2$-C≡C), 13.2 (s, 1C, **C**H$_3$-CH$_2$-C=CH$_2$), 14.2 (s, 1C, **C**H$_3$-CH$_2$-C≡C), 25.7 (s, 1C, **C**H$_2$-C=CH$_2$), 25.9 (s, 1C,

C≡C-**C**H_2-CH), 30.9 (s, 1C, **C**H_2-C=CH), 66.3 (s, 1C, O-**C**H_2), 72.7 (s, 1C, **C**H-O), 75.3 (s, 1C, CH_3-CH_2-C≡**C**), 83.6 (s, 1C, CH_3-CH_2-**C**≡C), 108.9 (s, 1C, C=**C**H_2), 121.3 (s, 1C, C=**C**H), 133.4 (s, 1C, **C**=CH), 148.2 (s, 1C, **C**=CH_2). MS (CI^+), *m/z* (%): 175.1 [M-C_2H_5]$^+$ (52), 161.1 [M-C_3H_5]$^+$ (42), 145.1 [M-C_4H_{11}]$^+$ (43), 137.1 [M-C_5H_7]$^+$ (58), 135.1 [M-C_5H_7]$^+$ (90), 119.1 [M-C_6H_{13}]$^+$ (44), 109.1 [C_7H_9O]$^+$ (100), 107.1 [C_7H_7O]$^+$ (39), 79.1 [C_7H_9]$^+$ (70). HRMS (CI^+): calcd. for $C_{14}H_{21}O$ ([M+H]$^+$) 205.1592, found 205.1593.

2-(Hex-2-yn-1-yl)-4-(pent-1-en-2-yl)-3,6-dihydro-2*H*-pyran (12d)

According to General procedure B, from oxaenediyne **2d** (25 mg, 0.11 mmol) in CH_2Cl_2 (1.5 mL) using **G-II** (4.6 mg, 5.4 μmol) in CH_2Cl_2 (1.5 mL) as a catalyst, dihydropyran **12d** of sufficient purity was obtained as a clear oil (24 mg, 95%). ^{1}H NMR: δ 0.92 (t, *J* = 7.3 Hz, 3H, C**H**$_3$-CH_2-CH_2-C=CH_2), 0.97 (t, *J* = 7.3 Hz, 3H, C**H**$_3$-CH_2-CH_2-C≡C), 1.40-1.58 (m, 4H, CH_3-C**H**$_2$), 2.15 (tt, *J* = 7.0 Hz, *J* = 2.5 Hz, 2H, CH_2-C**H**$_2$-C≡C), 2.17-2.41 (m, 4H, C**H**$_2$-C=CH + C**H**$_2$-C=CH_2), 2.43 (ddt, *J* = 16.4 Hz, *J* = 6.8 Hz, *J* = 2.4 Hz, 1H, C≡C-C**H**$_2$-CH), 2.52 (ddt, *J* = 16.4 Hz, *J* = 5.7 Hz, *J* = 2.4 Hz, 1H, C≡C-C**H**$_2$-CH), 3.58-3.68 (m, 1H, C**H**-O), 4.25-4.40 (m, 2H, O-C**H**$_2$), 4.90 (s, 1H, C=C**H**$_2$), 5.03 (s, 1H, C=C**H**$_2$), 5.79-5.85 (m, 1H, C=C**H**). ^{13}C NMR: δ 13.5 (s, 1C, **C**H_3-CH_2-CH_2-C≡C), 14.0 (s, 1C, **C**H_3-CH_2-CH_2-C=CH_2), 20.8 (s, 1C, CH_2-**C**H_2-C≡C), 21.9 (s, 1C, **C**H_2-CH_2-C=CH_2), 22.4 (s, 1C, **C**H_2-CH_2-C≡C), 26.0 (s, 1C, C≡C-**C**H_2-CH), 30.8 (s, 1C, **C**H_2-C=CH), 35.3 (s, 1C, **C**H_2-C=CH_2), 66.3 (s, 1C, O-**C**H_2), 72.7 (s, 1C, **C**H-O), 76.1 (s, 1C, CH_2-CH_2-C≡**C**), 82.1 (s, 1C, CH_2-CH_2-**C**≡C), 109.9 (s, 1C, C=**C**H_2), 121.4 (s, 1C, C=**C**H), 133.4 (s, 1C, **C**=CH), 146.6 (s, 1C, **C**=CH_2). MS (CI^+), *m/z* (%): 189.2 [M-C_3H_7]$^+$ (41), 151.1 [M-C_6H_9]$^+$ (51), 149.1 [M-C_6H_{11}]$^+$

(100), 133.1 [M-C_7H_{13}]$^+$ (47), 123.1 [M-C_8H_{13}]$^+$ (48), 107.1 [C_7H_7O]$^+$ (60), 81.1 [C_5H_5O]$^+$ (72). HRMS (CI$^+$): calcd. for $C_{16}H_{25}O$ ([M+H]$^+$) 233.1905, found 233.1902.

Methyl 4-[4-(3-methoxy-3-oxoprop-1-en-2-yl)-3,6-dihydro-2*H*-pyran-2-yl]but-2-ynoate (12e)

According to General procedure A, from oxaenediyne **2e** (32 mg, 0.12 mmol) in CH_2Cl_2 (1.3 mL) using **G-I** (5.0 mg, 6.1 μmol) in CH_2Cl_2 (1.3 mL) as a catalyst, dihydropyran **12e** of sufficient purity was obtained as a clear oil (20 mg, 63%). ^{1}H NMR: δ 2.23-2.34 (m, 2H, C**H**$_2$-C=CH), 2.62 (dd, *J* = 17.2 Hz, *J* = 6.6 Hz, 1H, C≡C-C**H**$_2$), 2.69 (dd, *J* = 17.2 Hz, *J* = 6.0 Hz, 1H, C≡C-C**H**$_2$), 3.77 (s, 3H, C**H**$_3$), 3.78-3.83 (m, 4H, C**H** + C**H**$_3$), 4.32-4.36 (m, 2H, O-C**H**$_2$), 5.62 (s, 1H, C=C**H**$_2$), 5.97 (s, 1H, C=C**H**$_2$), 6.12-6.15 (m, 1H, C=C**H**). ^{13}C NMR: δ 25.6 (s, 1C, **C**H$_2$-C≡C), 31.3 (s, 1C, **C**H$_2$-C=CH), 52.0 (s, 1C, **C**H$_3$), 52.6 (s, 1C, **C**H$_3$), 66.0 (s, 1C, O-**C**H$_2$), 71.0 (s, 1C, **C**H-O), 74.3 (s, 1C, C≡**C**-CH$_2$), 85.4 (s, 1C, CO-**C**≡C), 122.2 (s, 1C, C=**C**H$_2$), 126.2 (s, 1C, C=**C**H), 129.9 (s, 1C, CH=**C**), 140.6 (s, 1C, **C**=CH$_2$), 154.0 (s, 1C, C≡C-**C**=O), 167.1 (s, 1C, CH$_2$=C-**C**=O). MS (CI$^+$), *m/z* (%): 233.1 [M-CH_3O]$^+$ (100), 167.1 [M-$C_5H_5O_2$]$^+$ (65), 139.1 [M-$C_6H_5O_3$]$^+$ (49). HRMS (CI$^+$): calcd. for $C_{14}H_{17}O_5$ ([M+H]$^+$) 265.1076, found 265.1077.

4-[1-(Trimethylsilyl)ethenyl]-2-[3-(trimethylsilyl)prop-2-yn-1-yl]-3,6-dihydro-2*H*-pyran (12f)

According to General procedure A, from oxaenediyne **2f** (40 mg, 0.137 mmol) in CH_2Cl_2 (1.34 mL) under **G-I** (5.6 mg, 6.9 μmol) in CH_2Cl_2 (1.34 mL) catalysis, a mixture of the target product **12f** and the starting material **11** in a 1:4 ratio was obtained. The product could not be isolated in a pure state and was only identified in

^{1}H NMR spectra by comparison of the key signals with analogous compounds. ^{1}H NMR: δ 4.26-4.33 (m, 2H, O-C**H**$_2$), 5.38-5.40 (m, 1H, C=C**H**$_2$), 5.64-5.68 (m, 1H, C=C**H**$_2$), 5.71-5.74 (m, 1H, C=C**H**). Other ^{1}H NMR signals could not be convincingly assigned due to overlap with signals of the starting compound.

Diels-Alder reaction of dihydropyran **12b** with *N*-phenylmaleimide (**13**)

3-(But-2-yn-1-yl)-5-methyl-8-phenyl-3,4,6,6a,9a,9b-hexahydropyrano[3,4-e]isoindole-7,9(1*H*,8*H*)-dione (14)

Dihydropyran **12b** (100 mg, 0.567 mmol) and *N*-phenylmaleimide (**13**, 108 mg, 0.624 mmol) were dissolved in CH_2Cl_2 (4 mL) and the mixture was stirred for 130h at RT. After evaporation, the mixture was purified by gradient column chromatography (eluent hexane/EtOAc 2.5:1 $\rightarrow$ 2.4:1) to give major diastereomer (probably *endo-trans*-**14B**) (50 mg, 25%, white solid, Rf = 0.17 for hexane/EtOAc 2.5:1) and minor diastereomer (probably *exo-cis*-**14C** (28 mg, 14%, clear solid, Rf = 0.24 for hexane/EtOAc 2.5:1). A mixture of the two diastereomers (14 mg, 7%, **14B**/**14C** = 2:1) and some starting *N*-phenylmaleimide (58 mg, 54%) were also recovered.

Major diastereoisomer (probably *endo-trans*-**14B**): ^{1}H NMR: δ 1.76 (t, *J* = 2.6 Hz, 3H, C$\equiv$C-C**H**$_3$), 1.77 (s, 3H, C=C-C**H**$_3$), 2.22-2.42 (m, 4H, C$\equiv$C-C**H**$_2$ + C**H**$_2$-C=C-CH$_3$ + CH$_3$-C-C**H**$_2$), 2.58-2.67 (m, 2H, C**H**$_2$-C=C-CH$_3$ + O-CH$_2$-C**H**), 2.71 (dd, *J* = 14.5 Hz, *J* = 1.9 Hz, 1H, CH$_3$-C-C**H**$_2$), 3.19 (dd, *J* = 8.8 Hz, *J* = 6.9 Hz, 1H, CH-C**H**-C=O), 3.25-3.30 (m, 1H, CH$_2$-C**H**-C=O), 3.81-3.89 (m, 1H, C**H**-O), 3.95 (dd, *J* = 11.8 Hz, *J* = 5.7 Hz, 1H, O-C**H**$_2$), 4.46 (dd, *J* = 11.8 Hz, *J* = 8.1 Hz, 1H, O-C**H**$_2$), 7.17-7.20 (m, 2H, C$_{Ar}$-C**H**$_{Ar}$), 7.33-7.38 (m, 1H, C**H**$_{Ar}$), 7.40-7.46 (m, 2H, C**H**$_{Ar}$). ^{13}C NMR: δ 3.6 (s, 1C, C$\equiv$C-**C**H$_3$), 19.0 (s, 1C, C=C-**C**H$_3$), 26.6 (s, 1C, C$\equiv$C-**C**H$_2$), 28.9 (s, 1C, **C**H$_2$-C=C-CH$_3$), 30.6 (s, 1C, CH$_3$-C-**C**H$_2$), 37.1 (s, 1C, O-CH$_2$-**C**H), 40.7 (s, 1C, CH$_2$-**C**H-C=O),

42.1 (s, 1C, O-CH_2-CH-**C**H), 63.0 (s, 1C, O-**C**H_2), 72.9 (s, 1C, **C**H-O), 75.2 (s, 1C, CH_3-C≡**C**), 77.5 (s, 1C, CH_3-**C**≡C), 126.3 (s, 2C, C_{Ar}-**C**H_{Ar}), 127.4 (s, 1C, CH_3-C=**C**), 128.5 (s, 1C, **C**H_{Ar}), 129.0 (s, 1C, CH_3-**C**=C), 129.1 (s, 2C, **C**H_{Ar}), 131.9 (s, 1C, **C**$_{Ar}$), 176.8 (s, 1C, CH-CH-**C**=O), 178.5 (s, 1C, CH_2-CH-**C**=O). MS (ESI^+), *m/z* (%): 372.2 $[M+Na]^+$ (100), 350.2 $[M+H]^+$ (20). HRMS (ESI^+): calcd. for $C_{22}H_{24}O_3N$ ($[M+H]^+$) 350.1751, found 350.1752. HRMS (ESI^+): calcd. for $C_{22}H_{23}O_3NNa$ ($[M+Na]^+$) 372.1570, found 372.1571.

Minor diastereoisomer (probably *exo-cis*-**14C**): ^{1}H NMR: δ 1.72-1.76 (m, 3H, C=C-**C**H_3), 1.78 (t, *J* = 2.6 Hz, 3H, C≡C-C**H**$_3$), 2.16-2.45 (m, 4H, C≡C-C**H**$_2$ + C**H**$_2$-C=C-CH_3 + CH_3-C-C**H**$_2$), 2.53-2.74 (m, 3H, C**H**$_2$-C=C-CH_3 + O-CH_2-C**H** + CH_3-C-C**H**$_2$), 3.15-3.28 (m, 2H, CH-C**H**-C=O + CH_2-C**H**-C=O), 3.60-3.72 (m, 1H, C**H**-O), 4.16 (dd, *J* = 14.6 Hz, *J* = 11.7 Hz, 1H, O-C**H**$_2$), 4.19 (dd, *J* = 12.8 Hz, *J* = 11.7 Hz, 1H, O-C**H**$_2$), 7.16-7.22 (m, 2H, C_{Ar}-C**H**$_{Ar}$), 7.33-7.39 (m, 1H, C**H**$_{Ar}$), 7.40-7.48 (m, 2H, C**H**$_{Ar}$). ^{13}C NMR: δ 3.6 (s, 1C, C≡C-**C**H_3), 18.8 (s, 1C, C=C-**C**H_3), 26.4 (s, 1C, C≡C-**C**H_2), 30.3 (s, 1C, **C**H_2-C=C-CH_3), 30.7 (s, 1C, CH_3-C-**C**H_2), 35.6 (s, 1C, O-CH_2-**C**H), 40.1 (s, 1C, CH_2-**C**H-C=O), 40.9 (s, 1C, CH-**C**H-C=O), 66.3 (s, 1C, O-**C**H_2), 74.3 (s, 1C, **C**H-O), 75.0 (s, 1C, CH_3-C≡**C**), 77.5 (s, 1C, CH_3-**C**≡C), 126.3 (s, 2C, C_{Ar}-**C**H_{Ar}), 126.9 (s, 1C, CH_3-C=**C**), 127.7 (s, 1C, CH_3-**C**=C), 128.5 (s, 1C, **C**H_{Ar}), 129.1 (s, 2C, **C**H_{Ar}), 131.8 (s, 1C, **C**$_{Ar}$), 177.0 (s, 1C, CH-CH-**C**=O), 178.5 (s, 1C, CH_2-CH-**C**=O). MS (ESI^+), *m/z*: 372.2 $[M+Na]^+$ (100), 350.2 $[M+H]^+$ (35). HRMS (ESI^+): calcd. for $C_{22}H_{24}O_3N$ ($[M+H]^+$) 350.1751, found 350.1752. HRMS (ESI^+): calcd. for $C_{22}H_{23}O_3NNa$ ($[M+Na]^+$) 372.1570, found 372.1571.

Computational details

DFT calculations were performed using Gaussian16 program suite [35]**.** For visualizations, GaussView6 interface program was used [36]. Due to economy, pure

M06L functional [37], def2-SV(P) basis set [38] and resolution of identity approximation [39] were employed. Solvent (dichloromethane) was simulated using the SMD method [40].

Supporting Information

Supporting information contains copies of ^{1}H and ^{13}C NMR spectra of endiynes **2**, **10-11**, RCEYM products **12** and Diels-Alder reaction product **14**, as well as XYZ files of all computed structures (complexes **12b + 13**, products **14** and transition states **15**)

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