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From an Acyclic, Polyunsaturated Precursor to the Polycyclic Taxane Ring System: The [4+2]/[2+2+2] and [2+2+2]/[4+2] Cyclization Strategies

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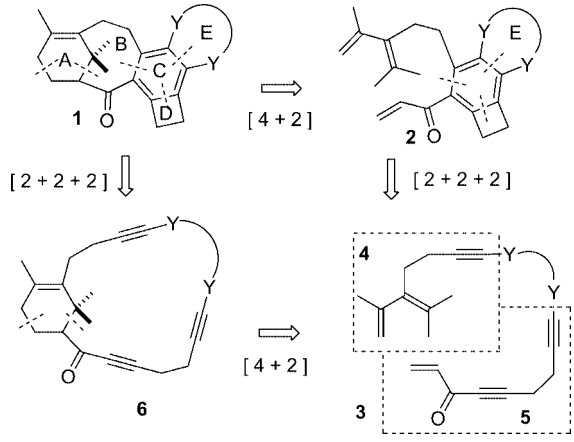
A combination of a cobalt(I)-mediated cyclotrimerization and a [4+2] reaction is described as a new entry into the ABC core of taxanes. The [4+2]/[2+2+2] and the [2+2+2]/[4+2] pathways both lead to the expected ABC core of the title compound. Mechanistic proposals are described to understand the formation of the side products during the [2+2+2] cycloaddition and to apply useful modifications of the highly substituted unsaturated precursors. Indeed, we demonstrate, for the first approach, that the substitution at the propargylic position has a dramatic influence on the cyclization. For the second sequence, we observe that the silicon group at the terminal position of the double bond can alter the chemoselectivity of the cycloaddition. In addition, the use of a temporary silicon tether in the [2+2+2] cycloaddition provides a rapid access to a highly elaborate molecule **38**, which exhibits latent functionality for further synthetic transformations.

Introduction

In 1971 Wall and Wani discovered a novel diterpenoid, taxol, and elucidated its unusual structure.[1] Shortly after its isolation, Horwitz and colleagues described taxol as a drug candidate that promotes the assembly of microtubules.[2] These two events stimulated different academic and industrial groups all around the world to synthesize taxol, and an impressive range of synthetic designs was proposed.[3] Interest in the total synthesis of taxol was triggered by the inherent complexity of this tetracyclic compound, which includes an eight-membered ring and a bridgehead double bond. To date, six total syntheses have been reported.[4]

In this context, we envisioned that a combination of a [4+2] cycloaddition and a cobalt(I)-mediated [2+2+2] cyclization, starting from easily prepared simple acyclic polyunsaturated partners, would allow a rapid construction of the tetracyclic skeleton of taxoids. Indeed, cobalt(I)-catalyzed cyclotrimerizations offer many possibilities and tolerance toward varied functional groups and their versatility in organic synthesis is an important feature that has already been widely demonstrated.[5]

Our strategy is depicted retrosynthetically in Scheme 1. We reasoned that compound **1**, which presents an aryl C-ring, an all carbon D-ring, and an additional E-ring, could be obtained from an intramolecular Diels–Alder reaction of the substrate **2**. The benzocyclobutene unit of **2** could arise from the [2+2+2] cyclization of the three alkynes of precursor **3**. The link between both unsaturated moieties **4** and **5** could be either an alkylated or a silylated tether, which should ensure the chemo- and regioselectivity of the [2+2+2] cyclizations.



Scheme 1.

Moreover, we have recently disclosed that the use of temporary silicon tethers (TST) is highly efficient in cobalt-catalyzed cyclotrimerizations and allows the formation of polysubstituted arenes, after the displacement of the silicon group.[6] Therefore, the functionalization of the aromatic C-ring appears feasible with this TST methodology.

Compound **1** could also be obtained by a reversed [4+2]/[2+2+2] sequence. The [2+2+2] cyclization could allow a

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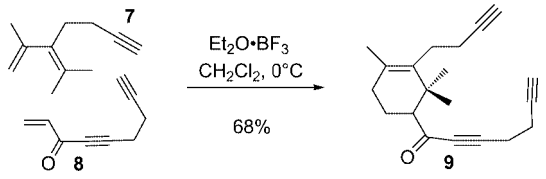
simultaneous formation of the A-, B-, and C-rings from compound **6**, and the latter could be formed by an intermolecular Diels–Alder reaction. The [4+2] reaction has already been successfully used by different groups in the approach to the taxane skeleton,[7] but never in combination with a cobalt(I)-mediated [2+2+2] cyclization.

In this paper we will document and discuss these two different approaches to the ABC core of taxanes that were achieved in our laboratory, and, moreover, we will conclude the section by applying our experience to the formation, the [2+2+2] cyclization, and the opening of silylated tethers.[8]

Results and Discussion

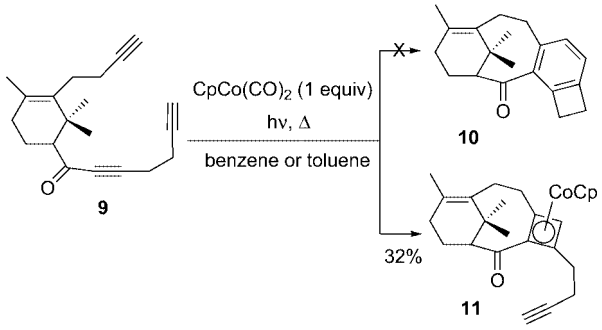
[4+2]/[2+2+2] Approach[8a]

The cycloadduct **9** was obtained in 68% yield upon treatment of compounds **7** and **8** with $Et_2O{\cdot}BF_3$ in dichloromethane at 0 °C (Scheme 2).



Scheme 2.

It was then submitted to "classical" conditions of cyclotrimerization: 5 mol-% of dicarbonyl(η^5-cyclopentadienyl)-cobalt [$CpCo(CO)_2$] in boiling xylenes, benzene, or toluene under irradiation (light from projector lamp; ELW, 300 W, 50% of its power). Surprisingly, this did not afford the desired pentacyclic compound **10**. However, when a stoichiometric amount of cobalt complex was used, the 6,8,4-tricyclic cyclobutadienyl complex **11** was obtained in 32% yield (Scheme 3). Its structure was established by an X-ray analysis[9] (Figure 1).



Scheme 3.

Complex **11** is photolytically and thermally quite inert and stable under oxidative conditions as well. The formation of such cyclobutadienes has been previously observed and is generally considered to arise when either coordination or insertion of the third alkyne component is problematic.[10]

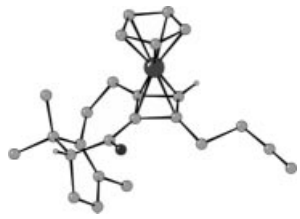
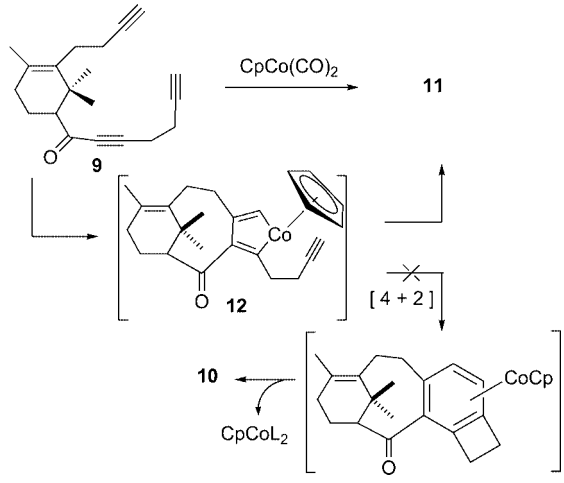


Figure 1. ORTEP representation of complex **11**.

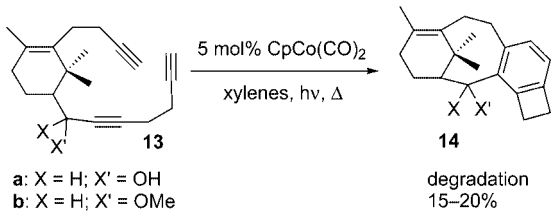
Its formation probably follows the general pathway[11] described in Scheme 4: after the coordination of the two triple bonds, the oxidative coupling could lead to the cobaltacyclopentadiene **12**. This presumed metallacycle intermediate would then prefer to isomerize to the complex **11** rather than to incorporate the appended alkyne unit. This is probably for electronic reasons due to the presence of the carbonyl group conjugated to the cyclopentadiene moiety.



Scheme 4.

We next investigated the cyclizations of the cyclohexatriynes **13** in which the carbonyl group at the propargylic position has been replaced by a hydroxy or a methoxy group. The results showed the dramatic influence of the substitution in that position. Thus, with a hydroxy group the reaction led only to the degradation of the starting material. It appeared that we could take advantage of a possible *gem*-disubstitution effect[12] in the cyclization by using an acetal group in that position, but despite intense efforts we were unable to introduce this kind of substituent either before, during, or after the [4+2] cycloaddition.

In contrast, in the case of a methoxy group we obtained the tetracyclic structure **14b** in 15–20% yield (Scheme 5), thus confirming the validity of the [4+2]/[2+2+2] approach to the taxane framework. Of course, the yield of the Co^I-mediated [2+2+2] cyclization would have to be improved but this strategy has shown that the cobalt(I) species is able to mediate the ring closure of strained polyunsaturated compounds into an eight-membered ring, which is sterically even more congested.

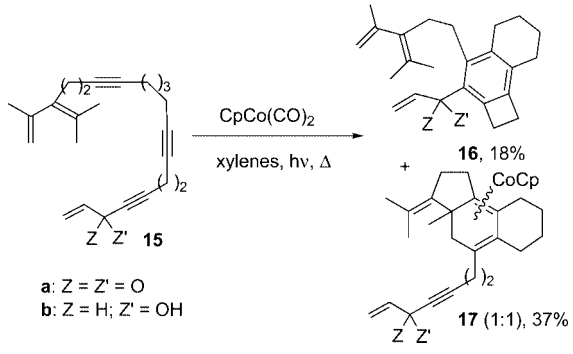


Scheme 5.

[2+2+2]/[4+2] Approach

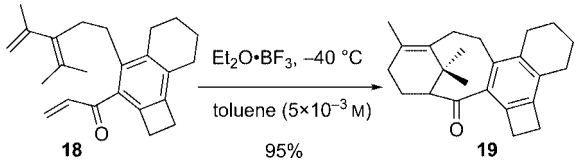
Alkylated Tether[8b]

At the same time we developed an alternative [2+2+2]/[4+2] approach. The cyclization of compound **15a**, substituted with a ketone at both the allylic and propargylic positions, led only to the decomposition of the latter. On the contrary, precursor **15b**, which has one hydroxy group at that position, gave the expected benzocyclobutene **16b** but in low yield (18%). Surprisingly, the major product was a 1:1 mixture of diastereomeric complexes **17b** (37%), arising from the [2+2+2] reaction between two alkynes and the terminal double bond (Scheme 6). The insertion of the last triple bond into the cobaltacyclopentadiene is probably disfavored for geometric reasons compared to that of the double bond. In addition, 30% of starting material **15b** remained unchanged. Attempts to avoid the participation of the double bond in the cyclization by a temporary protection of the diene system failed.



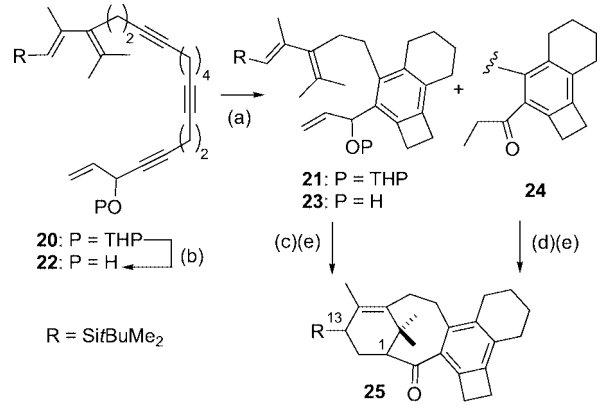
Scheme 6.

Nevertheless, **16b** was oxidized[7b] ($BaMnO_4$/Celite in benzene) and the [4+2] cyclization of **18** was performed in presence of $Et_2O{\cdot}BF_3$ at –40 °C in toluene, allowing the formation of the pentacyclic structure **19** in an excellent 95% yield (Scheme 7), thus validating the [2+2+2]/[4+2] approach to the taxane framework.



Scheme 7.

In order to avoid the competitive [2+2+2] reaction of the enediyne moiety, we then decided to introduce a bulky group at the terminal position of the double bond and we chose a silylated substituent (R = *t*BuMe$_2$Si) for this purpose. The presence of such a group was found to be very efficient, since when **20** was exposed to the cobalt mediator we were pleased to observe the formation of the corresponding benzocyclobutene **21** in 92% yield (Scheme 8). However, whatever conditions we used, we were unable to hydrolyze the tetrahydropyranyl ether of **21**.



Scheme 8. (a) 5 mol-% [$CpCo(CO)_2$], xylenes, Δ, hν; (b) cat. PTSA, MeOH, quantitative; (c) IBX, DMSO, room temp., 76%; (d) 1. LDA, PhSeBr, THF, 2. $NaIO_4$, $NaHCO_3$, MeOH/H_2O, 81%; (e) $Et_2O{\cdot}BF_3$, $CHCl_3$, –78 °C, 95%.

Under the same conditions, **22** led to a mixture of benzocyclobutenes **23** and **24** in 50 and 37% yield, respectively. Compound **24** presumably arises from a migration of the double bond leading to an enol. Moreover, the formation of **24** is not a problem because it can be easily converted into the dienophilic enone. Thus, after oxidation of **23** and selenation/oxidation/elimination of **24**, the resulting enone was treated with 5 equiv. of $Et_2O{\cdot}BF_3$ in chloroform to afford **25** in 95% yield as a single diastereomer of unidentified stereochemical arrangement.

As far as the [4+2] cyclization is concerned, molecular models reveal that only the *endo* approach is possible, and according to the chemical shifts of the three methyl groups (δ = 1.33, 1.12, 0.77 ppm), the conformation of the cycloadduct is probably *endo*, as described by Shea.[13]

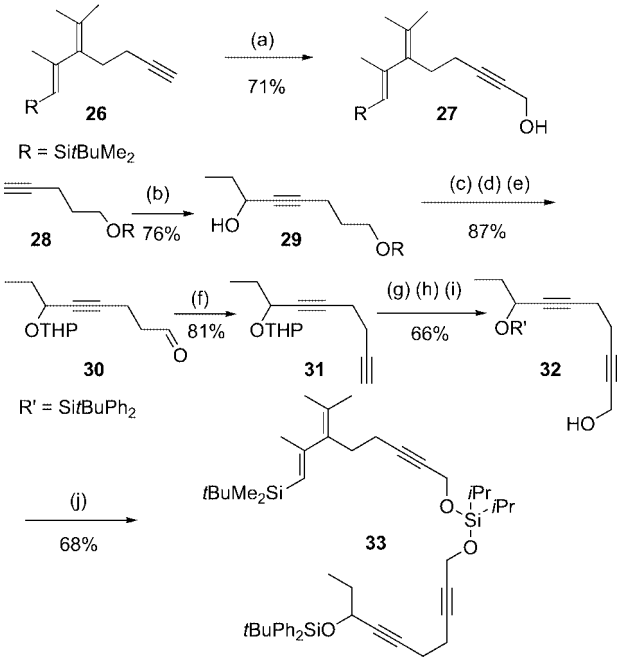
In summary, by circumventing the competitive reactions we have been able to perform the two key steps of our strategy in high yields and to show that a [2+2+2]/[4+2] approach is valid for the construction of the core of taxoids. However, the additional alkylated E-ring is a limiting factor for the functionalization of the aromatic C-ring. In relation with our studies on the use of TST in the [2+2+2] cyclizations, we turned our attention to a disposable silylated link connecting the unsaturated moieties **4** and **5**, which should ensure both the success of the [2+2+2] cyclization and further transformations of the cycloadducts.

Silylated Tether

In order to overcome all the previously encountered problems, namely the 1,3-migration of the double bond during the cobalt-mediated cyclization and the problematic hydrolysis of the THP ether at both the allylic and benzylic

positions, we envisioned the preparation of a new polyunsaturated precursor **33**. The latter presents a diisopropylsilaketal group and no allylic double bond.

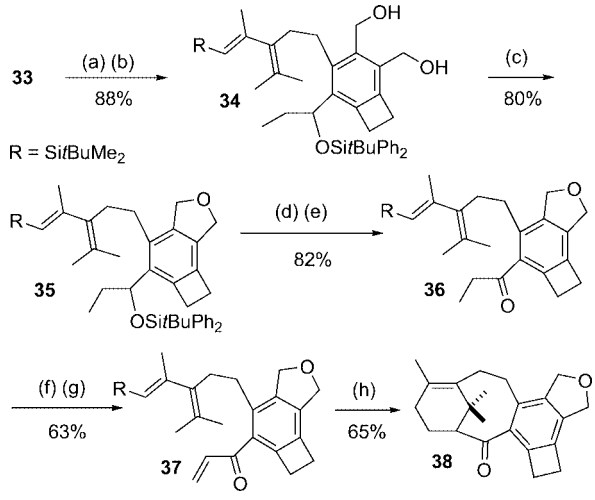
Similar to the preparation of **22**, the starting material for the synthesis is the dienyne **26**,[8b] which was alkylated with paraformaldehyde in 71% yield (Scheme 9).



Scheme 9. (a) *n*BuLi, THF, –78 °C, $(CH_2O)_n$; (b) *n*BuLi, THF, –78 °C, CH_3CH_2CHO, –78 °C to room temp.; (c) cat. PTSA, 3,4-dihydro-2*H*-pyran, CH_2Cl_2; (d) nBu_4NF, THF, 0 °C to room temp.; (e) SO_3·pyridine, DMSO, Et_3N, CH_2Cl_2, 0 °C; (f) $MeCOC(N_2)$-$P(O)(OMe)_2$ K_2CO_3, MeOH; (g) cat. PTSA, MeOH, room temp.; (h) tBuPh$_2$SiCl, Et_3N, 4-DMAP, CH_2Cl_2, room temp.; (i) *n*BuLi, –78 °C, THF, $(CH_2O)_n$, –78 °C to room temp.; (j) 1. Et_3N, 4-DMAP, CH_2Cl_2, room temp., ClSi*i*Pr$_2$H, 2. NBS, CH_2Cl_2, room temp., 3. **27**, Et_3N, 4-DMAP, CH_2Cl_2, room temp.

At the same time *tert*-butyldimethyl(pent-4-ynyloxy)silane (**28**) was alkylated with propanal in 76% yield and the resulting alcohol was protected as a tetrahydropyranyl ether (Scheme 9). After removal of the silylated group, the corresponding alcohol was oxidized to the aldehyde **30** in 87% yield over three steps. The transformation of **30** into the terminal alkyne was achieved in 81% yield by using the Ohira–Bestmann procedure.[14] Then, acid-catalyzed hydrolysis of the THP ether, further protection with a *tert*-butyldiphenylsilyl group, and hydroxyalkylation with paraformaldehyde furnished **32** in 66% yield over three steps. Finally, the silylated tether was introduced according to our reported procedure for the preparation of unsymmetrical silaketals.[15] This sequence is based upon the reaction of the alcohol **32** with chlorodiisopropylsilane, transformation of the resulting alkoxysilane into the corresponding bromide by reaction with *N*-bromosuccinimide, and condensation of the bromide with the second alcohol **27**. The resulting silaketal **33** was obtained in 68% yield and is stable to aqueous workup and chromatography on silica gel.

Treatment of **33** with 5 mol-% of $[CpCo(CO)_2]$ in boiling xylenes under irradiation led to the corresponding benzocyclobutene, which, after opening of the silaketal, afforded the diol **34** in 88% over two steps (Scheme 10).



Scheme 10. (a) 5 mol-% $[CpCo(CO)_2]$, xylenes, Δ, hv; (b) nBu_4NF (3 equiv.), THF, –78 to 0 °C; (c) *n*BuLi, THF, –78 °C, TsCl, –78 °C to room temp.; (d) nBu_4NF (1.2 equiv.), THF, reflux; (e) IBX, DMSO, room temp.; (f) NaHMDS, THF, –40 °C, PhSeCl, –40 °C to room temp.; (g) $NaIO_4$, $NaHCO_3$, MeOH/H_2O; (h) $Et_2O{\cdot}BF_3$ (5 equiv.), $CHCl_3$, –50 °C.

After monotosylation of **34**, tricyclic compound **35** was obtained in 80% yield. Subsequent treatment with nBu_4NF in refluxing THF, followed by oxidation of the resulting alcohol with *o*-iodoxybenzoic acid (IBX) in DMSO, afforded ketone **36**. Finally, the selenation/oxidation/elimination sequence described above provided the requisite enone **37**. The latter was treated with 5 equiv. of $Et_2O{\cdot}BF_3$ in chloroform to afford the desired cycloadduct **38** in 65% yield as a single diastereomer. According to the chemicals shifts of the three methyl groups (δ = 1.24, 1.18, 0.70 ppm), the conformation of the cycloadduct is *endo*.[13] This was unambiguously confirmed by a single-crystal X-ray analysis[9] (Figure 2).

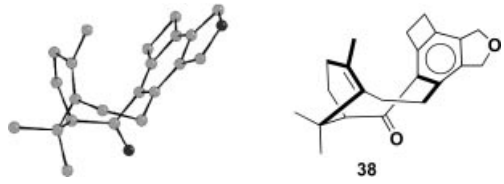


Figure 2. ORTEP representation of the cycloadduct **38**.

It should be noted that the cycloadduct undergoes a protodesilylation at C-13 in situ. As the *tert*-butyldimethylsilyl group is not suitable for a Fleming-[16] or Tamao–Kumada-type[17] oxidation, this protodesilylation is not troublesome, and therefore an allylic oxidation leading to the alcohol precursor of the lateral chain can be considered.[18]

Thus, the [2+2+2]/[4+2] approach to the core of taxoids has been validated with success. The yields of the two key steps of our strategy are very high either with the alkylated tether or the silylated one. The use of a temporary silicon tether greatly improves the reaction, and the transformation

of the aromatic C-ring of compound **38** can be now envisioned.

Conclusion

In this paper we have shown new examples of the remarkable synthetic potential of the combination of a cobalt(I)-mediated [2+2+2] cyclization with a [4+2] cycloaddition. More than just the formation of the skeleton of a natural product, we have studied here the behavior of highly functionalized unsaturated precursors in the presence of a cobalt(I) mediator and their transformations into strained polycyclic structures. In summary, the [4+2]/[2+2+2] approach to the taxane framework has been validated. It is obvious that the yield of the Co^{I}-mediated [2+2+2] cyclization has to be improved, but it is noteworthy that this approach has shown that cobalt species are able to mediate the ring closure of polyunsaturated compounds **9** and **13b** into an eight-membered ring containing a bridgehead double bond, which is sterically even more congested.

As for the [2+2+2]/[4+2] approach, the yields are good to excellent, no matter whether the link is an alkylated tether or a silylated one. The *endo* conformation of the pentacyclic structure **38** was established by a single-crystal X-ray analysis. In addition, the results have also described the compatibility of our previously reported method for the preparation of unsymmetrical silaketals with numerous and varied unsaturations. Finally, the most rewarding aspect of this approach was the ability to perform the cobalt-catalyzed cyclization with a temporary silicon tether, which allows a rapid entry to a compound (**38**) that has latent functionality for further synthetic transformations. Indeed, an allylic oxidation of C-13 to generate the corresponding alcohol, which is a precursor of the lateral chain, combined with an easy functionalization of the aromatic C-ring can be envisioned to lead to several analogs. In addition, this proposed strategy is a good opportunity for the preparation of a taxane skeleton with an all-carbon D-ring whose biological activity has never been evaluated due to the lack of methods of formation of such a ring.

Experimental Section

General Methods: All reactions were carried out under argon in flame-dried glassware, with magnetic stirring and degassed, anhydrous solvents. All commercially available reagents were used without further purification, unless otherwise noted. All solvents were reagent grade and distilled under a positive pressure of dry nitrogen before use. THF was distilled from sodium/benzophenone. Solid reagents were dried in vacuo (0.5–0.1 Torr). Thin layer chromatography (TLC) was performed on Merck 60 F_{254} silica gel. Merck Geduran SI 60-Å silica gel (35–70 μm) was used for column chromatography according to Still's method. PE and EE refer to petroleum ether and Et_2O. Chemical shifts are given in ppm, referenced to the residual proton resonances of the solvents (δ = 7.26 ppm for $CDCl_3$; δ = 7.16 ppm for C_6D_6). Coupling constants (J) are given in Hertz (Hz). Elemental analyses were performed by the Service Régional de Microanalyse de l'Université Pierre et Marie Curie. Low-resolution mass spectra (MS) and high-resolution mass spectra (HRMS) were measured by the Service de spectrométrie de masse de l'ICSN-CNRS, Gif-sur-Yvette. IR spectra were recorded with a Bruker Tensor 27 spectrometer. Absorbance frequencies are given at maximum of intensity in cm^{-1}.

[4+2]/[2+2+2] Approach: Characterization data for **7**, **8**, **9**, and **11** have already been reported.[8a,8b]

1-(3-But-3-ynyl-2,2,4-trimethylcyclohex-3-enyl)hepta-2,6-diyn-1-ol (13a): Cerium(III) chloride (0.180 g, 0.73 mmol) and then sodium borohydride (0.028 g, 0.73 mmol) were added to a cooled (–78 °C) solution of ketone **9** (0.205 g, 0.73 mmol) in methanol (3.6 mL). The reaction mixture was then diluted with Et_2O and hydrolyzed with H_2O. The organic layer was dried with magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (PE/EE = 80:20) to give the alcohol **13a** as a mixture of diastereomers (*de* = 93%). Only the major isomer of **13a** (0.196 g, 95%) was characterized. IR (neat): $\tilde{\nu}$ = 3500, 3300, 2920, 2100, 1470, 1430, 1380, 1365, 1040, 640 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 21 °C): δ = 1.03 [s, 3 H, $C(CH_3)_2$], 1.11 [s, 3 H, $C(CH_3)_2$], 1.54 [dt, J = 10.9, 2.3 Hz, 1 H, CH_2–CH–CH(OH)–], 1.65 (s, 3 H, CH_3–C=), 1.68–1.77 (m, 1 H, CH_2–CH), 1.83–1.87 (m, 1 H, CH_2–CH), 2.00 (t, J = 2.5 Hz, 1 H, ≡CH), 2.03 [t, J = 2.5 Hz, 1 H, C≡$C(CH_2)_2C$≡CH], 2.02–2.08 (m, 2 H, C≡C–CH_2–CH_2–C≡CH), 2.18–2.24 (m, 2 H, CH_2–C≡CH), 2.25–2.34 (m, 2 H, CH_2–CH_2–C≡CH), 2.38–2.48 (m, 4 H, C≡C–CH_2–CH_2–C≡CH, =C–CH_2–), 4.58 (br. s, 1 H, CH–OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): δ = 18.7 (CH_2), 18.8 (2 CH_2), 19.3 (CH_2), 20.1 (CH_3), 22.9 (CH_3), 27.5 (CH_3), 28.1 (CH_2), 32.1 (CH_2), 38.1 (C), 51.2 (CH–OH), 62.8 (CH), 68.2 (C), 69.3 (C), 82.6 (CH), 82.7 (C), 83.3 (C), 84.6 (CH), 129.2 (C), 136.0 (C) ppm.

2-But-3-ynyl-4-(1-methoxyhepta-2,6-diynyl)-1,3,3-trimethylcyclohexene (13b): At 0 °C, a solution of alcohol **13a** (0.30 g, 1.06 mmol) in THF (3 mL) was added dropwise to a suspension of sodium hydride (60% in oil, 42.4 mg, 1.06 mmol) in THF (2 mL). After being stirred at room temperature for 30 min, methyl iodide (0.33 mL, 5.3 mmol) was added and the resulting mixture was stirred for an additional hour. The solution was then diluted with Et_2O and washed with a saturated solution of ammonium chloride and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (PE/EE = 90:10) to give the ether **13b** (0.268 g, 85%) as a colorless oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 3300, 2980, 2950, 2100, 1660, 1610, 1440, 1250, 930 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 21 °C): δ = 0.91 [s, 3 H, $C(CH_3)_2$], 1.07 [s, 3 H, $C(CH_3)_2$], 1.53–1.56 [m, 1 H, CH_2–CH–CH(OMe)–], 1.63 (s, 3 H, CH_3–C=), 1.80–2.06 [m, 4 H, =C–$(CH_2)_2$], 1.97 (t, J = 2.5 Hz, 1 H, ≡CH), 2.00 [t, J = 2.5 Hz, 1 H, C≡$C(CH_2)_2C$≡CH], 2.14–2.31 (m, 4 H, CH_2–CH_2–C≡CH), 2.37–2.47 [m, 4 H, C≡$C(CH_2)_2C$≡CH], 3.32 (s, 3 H, CH_3O), 4.04 (d, J = 1.5 Hz, 1 H, –CH–OMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): δ = 18.7 (2 CH_2), 19.2 (CH_2), 19.4 (CH_2), 19.9 (CH_3), 22.4 (CH_3), 27.0 (CH_3), 28.2 (CH_2), 32.5 (CH_2), 38.2 (C), 51.1 (CH), 56.1 (CH_3O), 68.1 (CH), 69.2 (CH), 71.6 (CH), 81.0 (C), 82.4 (C), 83.1 (C), 84.5 (C), 128.5 (C), 135.9 (C) ppm.

Cycloadduct 14b: Dicarbonyl(cyclopentadienyl)cobalt(I) (0.05 equiv.) was added to a boiling solution of **13b** (0.10 g, 0.33 mmol) in xylenes (15 mL) degassed by three freeze-pump-thaw cycles and was irradiated (light projector lamp: ELW, 300 W, 50% of its power). The reaction was monitored by TLC and, after completion, the reaction mixture was concentrated in vacuo. The crude mixture was purified by flash chromatography on silica (PE/EE = 90:10) to give **14b** (0.16 g, 16%) as a yellow oil. IR (CH_2Cl_2): $\tilde{\nu}$ = 2970, 1700, 1450, 1370, 1090 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$,

21 °C): δ = 0.30 [s, 3 H, C(CH_3)$_2$], 0.99 [s, 3 H, C(CH_3)$_2$], 1.64 (s, 3 H, CH_3–C=), 1.10–2.71 [m, 9 H, –C*H*–CH(OMe), =C–(CH_2)$_2$–CH, =C–(CH_2)$_2$–C=], 3.00 [t, J = 4.2 Hz, 2 H, CH_2(cyclobutene)], 3.10 (s, 3 H, CH_3O), 3.22–3.28 [m, 2 H, CH_2(cyclobutene)], 3.77 (d, J = 8.6 Hz, 1 H, –C*H*–OMe), 6.84 (d, J = 7.3 Hz, 1 H, H arom), 6.91 (d, J = 7.3 Hz, 1 H, H arom) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): δ = 18.8 (CH_3), 21.5 (CH_2), 21.7 (CH_3), 26.3 (CH_3), 27.1 (CH_2), 29.9 (CH_2), 31.2 (CH_2), 31.7 (CH_2), 32.5 (CH_2), 38.2 (C), 57.0 (CH_3), 57.1 (CH), 84.4 (CH), 122.2 (CH), 126.0 (C), 130.4 (CH), 137.7 (C), 140.3 (C), 140.4 (C), 144.3 (C), 144.9 (C) ppm.

[2+2+2]/[4+2] Approach: Characterization data of compounds **15**–**26** have already been reported.[8b]

6-[2-(*tert*-Butyldimethylsilyl)-1-methylvinyl]-7-methyloct-6-en-2-yn-1-ol (27): *n*BuLi (2.3 M solution in pentane, 1.8 mL, 4.20 mmol) was added dropwise to a cooled (–78 °C) solution of compound **26** (1.17 g, 4.00 mmol) in THF (7 mL). After being stirred at this temperature for 15 min, paraformaldehyde (0.12 mmol, 3.60 g) was added. The solution was warmed to room temperature and stirred until completion of the reaction (TLC). The solution was then diluted with Et_2O and washed with a saturated solution of ammonium chloride and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (PE/EE = 90:10) to give the alcohol **27** (0.83 g, 71%) as a colorless oil. IR (neat): $\tilde{\nu}$ = 3300, 2980, 2950, 2100, 1660, 1610, 1440, 1250, 930 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 21 °C): δ = 0.10 [s, 6 H, Si(CH_3)$_2$], 0.90 [s, 9 H, SiC(CH_3)$_3$], 1.65 [s, 3 H, C=C(CH_3)$_2$], 1.69 [s, 3 H, C=C(CH_3)$_2$], 1.80 [s, 3 H, CH=C(CH_3)–], 2.21 (m, 2 H, CH_2–C≡), 2.33 (m, 2 H, =C–CH_2), 4.25 (m, 2 H, CH_2–OH), 5.08 (s, 1 H, *H*C=) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): δ = 4.2 (2 CH_3), 17.3 (C), 17.9 (CH_2), 19.5 (CH_3), 21.7 (2 CH_3), 26.5(3 CH_3), 30.1 (CH_2), 51.2 (CH_2OH), 65.9 (C), 78.1 (C), 124.8 (C), 125.1 (=CH), 139.3 (C), 155.6 (C) ppm. $C_{18}H_{32}OSi$ (292.53): calcd. C 73.90, H 11.03; found C 73.93, H 11.35.

8-(*tert*-Butyldimethylsilyloxy)oct-4-yn-3-ol (29): *n*BuLi (2.3 M solution in pentane, 43.0 mL, 99.0 mmol) was added dropwise to a cooled (–78 °C) solution of 5-(*tert*-butyldimethylsilyloxy)pent-4-yne[19] (17.85 g, 90.0 mmol) in THF (138 mL). After being stirred at this temperature for 20 min, propanal (7.1 mL, 99.0 mmol) was added. The solution was warmed up to room temperature and stirred until completion of the reaction (TLC). The solution was then diluted with Et_2O and washed with a saturated solution of ammonium chloride and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was purified by flash chromatography on silica gel (PE/EE = 90:10) and gave **29** (17.63 g, 76%) as a yellow oil. IR (neat): $\tilde{\nu}$ = 3500, 2850, 2100, 1450, 1395, 1110, 860 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 21 °C): δ = 0.05 [s, 6 H, Si(CH_3)$_2$], 0.89 [s, 9 H, SiC(CH_3)$_3$], 0.98 (m, 3 H, CH_3–CH_2), 1.65–1.73 (m, 4 H, Me–CH_2, CH_2–CH_2–CH_2), 2.28 (m, 2 H, CH_2–CH_2–CH_2), 3.68 (t, J = 3.6 Hz, 2 H, –CH_2OSi), 4.28 (br. s, 1 H, C*H*OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): δ = –5.0 (2 CH_3), 9.8 (CH_3), 18.7 (C), 15.4 (CH_2), 26.3 (3 CH_3), 31.5 (CH_2), 32.0 (CH_2), 61.9 (CH_2–O), 64.2 (CH–OH), 81.6 (C), 85.2 (C) ppm.

6-(Tetrahydropyran-2-yloxy)oct-4-ynal (30): 3,4-Dihydro-2*H*-pyran (6.6 mL, 72.1 mmol) and *p*-toluenesulfonic acid (PTSA) (130 mg, 0.7 mmol) were added to a solution of **29** (68.63 mmol) in CH_2Cl_2 (69 mL). The mixture was stirred until completion of the reaction (TLC). The solution was extracted with Et_2O, washed with a saturated solution of $NaHCO_3$ and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was used without further purification in the next step. Tetrabutylammonium fluoride (1 M solution in THF, 75.5 mL, 75.5 mmol) was added dropwise to a cooled (0 °C) solution of the preceding compound (68.7 mmol) in THF (500 mL). The solution was warmed up to room temperature and stirred until completion of the reaction (TLC). The reaction mixture was extracted with Et_2O, washed with brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was used without further purification in the next step. DMSO (87 mL, 1220.1 mmol), triethylamine (85 mL, 610.5 mmol) and the complex pyridine/SO_3 (50.92 g, 366.3 mmol) were added to a cooled (0 °C) solution of the preceding alcohol (13.82 g, 61.1 mmol) in CH_2Cl_2 (110 mL). The mixture was stirred at 0 °C until TLC indicated completion of the reaction. The solution was diluted with Et_2O, washed with a saturated solution of NH_4Cl and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (PE/EE = 85:15) to give the aldehyde **30** (13.33 g, 87% over 3 steps) as a mixture of two diastereomers. IR (neat): $\tilde{\nu}$ = 2940, 2100, 1765, 930 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 21 °C): **30a**: δ = 0.97 (m, 3 H, CH_3–CH_2), 1.50–1.82 [m, 8 H, 3×CH_2(THP), Me–CH_2], 2.51 (m, 2 H, –CH_2–CH_2–), 2.63 (m, 2 H, –CH_2–CH_2–CHO), 3.48 (m, 1 H, C*H*–OTHP), 3.77 [m, 1 H, C*H*–O(THP)], 4.28 [m, 1 H, C*H*–O(THP)], 4.90 (m, 1 H, O–C*H*–O), 9.75 (s, 1 H, –HC=O) ppm; **30b**: δ = 0.93 (m, 3 H, CH_3–CH_2), 1.50–1.82 [m, 8 H, 3×CH_2(THP), Me–CH_2], 2.51 [m, 2 H, –CH_2–CH_2–], 2.63 (m, 2 H, –CH_2–CH_2–CHO), 3.48 (m, 1 H, C*H*–OTHP), 3.95 [m, 1 H, C*H*–O(THP)], 4.18 [m, 1 H, C*H*–O(THP)], 4.68 (m, 1 H, O–C*H*–O), 9.75 (s, 1 H, –*H*C=O) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): **30a**: δ = 9.96 (CH_3), 12.1 (CH_2), 19.4 (CH_2), 25.5 (CH_2), 29.2 (CH_2), 30.5 (CH_2), 42.7 (CH_2), 62.2 (CH_2), 66.2 (CH–O), 68.5 (CH–O), 81.0 (C≡), 83.6 (C≡), 200.6 (–HC=O) ppm; **30b**: δ = 9.55 (CH_3), 12.2 (CH_2), 19.4 (CH_2), 25.4 (CH_2), 28.7 (CH_2), 30.5 (CH_2), 42.7 (CH_2), 62.4 (CH_2), 66.2 (CH–O), 68.5 (CH–O), 80.0 (C≡), 82.8 (C≡), 200.4 (–HC=O) ppm.

3-(Tetrahydropyran-2-yloxy)nona-4,8-diyne (31): K_2CO_3 (16.42 g, 118.8 mmol) and a solution of dimethyl (1-diazo-2-oxopropyl)-phosphonate (13.70 g, 71.3 mmol) in MeOH (120 mL) were added to a solution of **30** (59.4 mmol, 1.0 equiv.) in MeOH (330 mL) and the mixture was stirred at room temperature for 6 h. The solution was diluted with Et_2O, washed with a saturated solution of NH_4Cl followed with brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was purified by flash chromatography (PE/EE = 98:2) to give compound **31** (10.65 g, 81%) as a mixture of two diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$, 21 °C): **31a**: δ = 0.98 (t, J = 7.6 Hz, 3 H, CH_3–CH_2), 1.15–1.70 [m, 8 H, 3×CH_2(THP), Me–CH_2], 1.97–1.98 (m, 1 H, ≡CH), 2.34–2.42 [m, 4 H, ≡C–(CH_2)$_2$–C≡], 3.46–3.49 (m, 1 H, C*H*–OTHP), 3.76 [br. t, J = 9.0 Hz, 1 H, C*H*–O(THP)], 4.29 [dt, J = 6.6, 1.6 Hz, 1 H, C*H*–O(THP)], 4.94 (br. s, 1 H, O–C*H*–O) ppm; **31b**: δ = 0.96 (t, J = 7.6 Hz, 3 H, CH_3–CH_2), 1.70–1.15 [m, 8 H, 3×CH_2(THP), Me–CH_2], 1.97–1.98 (m, 1 H, ≡CH), 2.34–2.42 [m, 4 H, ≡C–(CH_2)$_2$–C≡], 3.46–3.49 (m, 1 H, C*H*–OTHP), 3.97 [br. t, J = 9.0 Hz, 1 H, C*H*–O(THP)], 4.19 [dt, J = 6.2, 1.6 Hz, 1 H, C*H*–O(THP)], 4.70 (br. s, 1 H, O–C*H*–O) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): **31a**: δ = 10.2 (CH_3), 19.2 (2 CH_2), 19.7 (CH_2), 25.9 (CH_2), 29.4 (CH_2), 30.8 (CH_2), 62.5 (CH_2), 66.6 (CH–O), 69.5 (≡*C*H), 80.4 (–C≡), 82.9 (–C≡), 84.0 (–C≡), 95.6 (O–CH–O) ppm; **31b**: δ = 9.8 (CH_3), 19.3 (2 CH_2), 19.5 (CH_2), 25.7 (CH_2), 29.1 (CH_2), 30.8 (CH_2), 62.5 (CH_2), 66.7 (CH–O), 69.6 (–C≡*C*H), 81.3 (–C≡), 83.0 (–C≡), 83.3 (–C≡), 98.0 (O–CH–O) ppm.

8-(*tert*-Butyldiphenylsilyloxy)deca-9–2,6-diyn-1-ol (32): PTSA (92 mg, 0.5 mmol) was added to a solution of **31** (10.65 g, 48.3 mmol) in MeOH (84 mL). The mixture was stirred at room temperature until completion of the reaction (TLC). The solution was diluted with Et_2O, washed with a saturated solution of

$NaHCO_3$ and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude mixture was used without further purification in the next step. Triethylamine (6.8 mL, 49.3 mmol), 4-(dimethylamino)pyridine (4-DMAP) (547 mg, 4.5 mmol), and *tert*-butyldiphenylsilyl chloride (12.3 mL, 47.0 mmol) were added to a solution of the preceding alcohol (0.61 g, 44.8 mmol) in CH_2Cl_2 (100 mL). The mixture was stirred at room temperature until TLC indicated completion of the reaction. The solution was diluted with Et_2O, washed with a saturated solution of NH_4Cl and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was used without further purification in the next step. *n*BuLi (2.2 M solution in pentane, 19.1 mL, 41.4 mmol) was added dropwise to a cooled (–78 °C) solution of the preceding compound (14.76 g, 39.4 mmol) in THF (60 mL). After being stirred at this temperature for 20 min, paraformaldehyde (3.55 g, 118.2 mmol) was added. The solution was warmed up to room temperature and stirred until completion of the reaction (TLC). The solution was then diluted with Et_2O, washed with a saturated solution of ammonium chloride and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was purified by flash chromatography on silica gel (PE/EE = 90:10) to give **32** (12.87 g, 66% over 3 steps) as a colorless oil. IR (neat): $\tilde{\nu}$ = 3329, 2931, 2857, 2100, 1427, 1109, 1006, 821, 700, 611 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 21 °C): δ = 0.81 (t, J = 7.1 Hz, 3 H, CH_3–CH_2), 0.94 [br. s, 9 H, $SiC(CH_3)_3$], 1.54 (m, 2 H, Me–CH_2–), 2.10 [m, 4 H, ≡C–$(CH_2)_2$–C≡], 4.07 (m, 2 H, CH_2OH), 4.17 (m, 1 H, C*H*–OSi), 7.25 [m, 6 H, 2×3 *H*(Ph)], 7.45–7.63 [m, 4 H, 2×2 *H*(Ph)] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): δ = 9.7 (CH_3), 19.2 (CH_2), 19.7 (C), 27.4 (3 CH_3), 32.0 (2 CH_2), 51.6 (CH_2OH), 65.6 (CH), 79.6 (C), 82.9 (C), 83.8 (C), 85.1 (C), 127.7 (2 CH), 128.0 (2 CH), 129.9 (CH), 130.1 (CH), 134.5(2 C), 136.2 (2 CH), 136.4 (2 CH) ppm. $C_{26}H_{32}O_2Si$ (404.62): calcd. C 77.18, H 7.97; found C 77.33, H 8.20.

Silaketal Tether 33: Triethylamine (0.4 mL, 2.93 mmol), 4-DMAP (26 mg, 0.21 mmol), and chlorodiisopropylsilane (0.50 mL, 2.93 mmol) were added to a solution of alcohol **32** (1.02 g, 2.51 mmol) in CH_2Cl_2 (25 mL). The mixture was stirred at room temperature until completion of the reaction (TLC). This solution was then transferred under argon with filtration into another flask, and NBS (447 mg, 2.51 mmol) was added slowly. The resulting mixture was stirred until completion of the reaction (TLC). Finally, the preceding solution was added to a solution of alcohol **27** (613 mg, 2.09 mmol) in the presence of triethylamine (0.35 mL, 2.51 mmol) and 4-DMAP (26 mg, 0.21 mmol) in CH_2Cl_2 (25 mL). The mixture was stirred at room temperature until completion of the reaction (TLC). After concentration in vacuo, the residue was purified by flash chromatography on silica gel (PE/EE = 99:1) to give **33** (1.15 g, 68%) as a yellow oil. IR (neat): $\tilde{\nu}$ = 3000, 2940, 2320, 1590, 1050, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 21 °C): δ = 0.12 [s, 6 H, $Si(CH_3)_2tBu$], 0.92 [s, 9 H, $SiC(CH_3)_3$], 0.99 (t, J = 6.0 Hz, 3 H, CH_3–CH_2), 1.10 [br. s, 23 H (9 H + 2×7 H), $SiC(CH_3)_3$, $SiiPr_2$], 1.66 [s, 3 H, $=C(CH_3)_2$], 1.70 [s, 3 H, $=C(CH_3)_2$], 1.82 [s, 3 H, $=C(CH_3)$–], 2.37–2.22 [m, 10 H, 5×CH_2, =C–$(CH_2)_2$–C≡, ≡C–$(CH_2)_2$–C≡, CH_2–Me], 4.32 (t, J = 1.2 Hz, 1 H, C*H*–$OSiPh_2tBu$), 4.44 (br. s, 4 H, ≡C–CH_2–$OSiiPr_2O$–CH_2–C≡), 5.11 (s, 1 H, –C*H*=), 7.38–7.45 [m, 6 H, 2×3 H(Ph)], 7.79–7.71 [m, 4 H, 2×2 H(Ph)]. HRMS calcd. for $C_{50}H_{76}O_3Si_3$ [MNH_4^+]: 826.5446; found 826.5455.

[4-{3-[2-(*tert*-Butyldimethylsilyl)-1-methylvinyl]-4-methylpent-3-enyl}-5-{1-(*tert*-butyldiphenylsilyloxy)propyl}-2-(hydroxymethyl)bicyclo[4.2.0]octa-1,3,5-trien-3-yl]methanol (34): Dicarbonyl(cyclopentadienyl)cobalt(I) (0.05 equiv.) was added to a boiling solution of **33** (1.12 g, 1.39 mmol) in xylenes (75 mL) degassed by three freeze-pump-thaw cycles and was irradiated (light projector lamp: ELW, 300 W, 50% of its power). The reaction was monitored by TLC, and after completion, the reaction mixture was concentrated in vacuo. The crude mixture was filtered through a Celite pad and used without further purification in the next step. Tetrabutylammonium fluoride (1 M solution in THF, 4.17 mL, 4.17 mmol) was added dropwise to a cooled (–78 °C) solution of the preceding compound in THF (16 mL). The solution was warmed to 0 °C and stirred until completion of the reaction (TLC). The solution was then diluted with Et_2O, washed with a saturated solution of ammonium chloride and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was purified by flash chromatography to give compound **34** (875 mg, 88% over 2 steps) as a yellow oil. IR (ATR): $\tilde{\nu}$ = 3329, 2927, 2857, 1742, 1599, 1055, 823, 700 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$, 21 °C): δ = 0.13 [s, 6 H, $Si(CH_3)_2tBu$], 0.94 [m, 11 H, $SiC(CH_3)_3Me_2$, CH_2], 1.07 [m, 12 H, $SiC(CH_3)_3Ph_2$, CH_3], 1.44 [s, 3 H, $=C(CH_3)_2$], 1.62 [s, 3 H, $=C(CH_3)_2$], 1.75 [s, 3 H, $=C(CH_3)_2$], 2.00 (m, 2 H, CH_2–CH_2), 2.34 (m, 2 H, CH_2–CH_2), 3.15 [m, 2 H, CH_2(cyclobutene)], 3.38 [m, 3 H, CH_2(cyclobutene), C*H*–OSi], 4.17 (br. s, 4 H, 2×CH_2OH), 5.09 (br. s, 1 H, –C*H*=), 7.44–7.09 [m, 8 H, 2×4 H(Ph)], 7.69 [d, J = 6.8 Hz, 2 H, 2×1 H(Ph)]. HRMS calcd. for $C_{44}H_{64}O_3Si_2$ [MNH_4^+]: 714.4738; found 714.4755.

4-{3-[2-(*tert*-Butyldimethylsilyl)-1-methylvinyl]-4-methylpent-3-enyl}-3-[1-(*tert*-butyldiphenylsilyloxy)propyl]-1,2,5,7-tetrahydro-6-oxacyclobuta[*e*]indene (35): *n*BuLi (2.2 M solution in pentane, 0.13 mL, 0.29 mmol) was added dropwise to a cooled (–78 °C) solution of **34** (100 mg, 0.14 mmol) in THF (3 mL). After being stirred at this temperature for 30 min, tosyl chloride (27 mg, 0.14 mmol) was added. The solution was warmed to room temperature and stirred until completion of the reaction (TLC). The solution was then diluted with Et_2O, washed with a saturated solution of ammonium chloride and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was purified by flash chromatography on silica gel (PE/EE = 95:5) to give **35** (78 mg, 80%) as a yellow oil. IR (neat): $\tilde{\nu}$ = 3030, 2920, 1625, 1462, 1054, 822, 739 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 21 °C): δ = 0.14 [s, 6 H, $Si(CH_3)_2tBu$], 0.94 [br. s, 12 H, $SiC(CH_3)_3Me_2$, CH_3–CH_2], 1.08 [br. s, 11 H, $SiC(CH_3)_3Ph_2$, Me–CH_2], 1.30 [s, 3 H, $=C(CH_3)_2$], 1.62 [s, 3 H, $=C(CH_3)_2$], 1.74 [s, 3 H, $=C(CH_3)$], 1.88–2.08 (m, 4 H, –CH_2–CH_2–), 3.06 [m, 2 H, CH_2(cyclobutene)], 3.41 [m, 3 H, CH_2(cyclobutene), C*H*–OSi], 5.13–4.93 (m, 5 H, CH_2–O–CH_2, CH=), 7.69–7.02 [m, 10 H, 2×5 H(Ph)] ppm. $C_{44}H_{62}O_2Si_2$ (679.13): calcd. C 77.82, H 9.20; found C 77.93, H 9.59.

1-(4-{3-[2-(*tert*-Butyldimethylsilyl)-1-methylvinyl]-4-methylpent-3-enyl}-1,2,5,7-tetrahydro-6-oxacyclobuta[*e*]inden-3-yl)propan-1-one (36): Tetrabutylammonium fluoride (1 M solution in THF, 1.06 mL, 1.06 mmol) was added dropwise to a solution of **35** (601 mg, 0.88 mmol) in THF (11 mL). The solution was stirred and refluxed until TLC indicated completion of the reaction. The reaction mixture was extracted with Et_2O, washed with a saturated solution of ammonium chloride and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was used without further purification in the next step. IBX (474 mg, 1.77 mmol) was added to a solution of the preceding compound in DMSO (9 mL). The mixture was stirred until completion of the reaction (TLC). The solution was washed with water, filtered through a Celite pad, diluted with Et_2O, washed with brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was purified by flash chromatography to give compound **36** (320 mg, 82% over 2 steps) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$, 21 °C): δ = 0.16 [s, 6 H, $Si(CH_3)_2tBu$] 0.95 [s, 9 H, $SiC(CH_3)_3Me_2$], 1.20 (t, J = 7.1 Hz, 3 H, CH_3–CH_2), 1.69 [s, 3 H, $=C(CH_3)_2$], 1.80 [s, 3 H,

=C(CH_3)$_2$], 1.88 [s, 3 H, =C(CH_3)], 2.30 (m, 2 H, CH_2–CH_2), 2.70 (m, 2 H, CH_2–CH_2), 2.75 (q, J = 7.1 Hz, 2 H, Me–CH_2–), 3.15 [m, 2 H, CH_2(cyclobutene)], 3.41 [m, 2 H, CH_2(cyclobutene)], 5.07 (br. s, 4 H, CH_2–O–CH_2), 5.15 (s, 1 H, –CH=) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): δ = –4.1 (2 CH_3), 8.2 (CH_3), 17.4 (C), 19.5 (3 CH_3), 21.8 (CH_3), 22.0 (CH_3), 26.7 (CH_3), 28.0 [CH_2–C(O)], 30.7 (CH_2), 32.3 (CH_2), 32.4 (CH_2), 36.8 (CH_2), 72.1 (CH_2–O–), 72.8 (CH_2–O–), 124.0, 124.7 (*C*H=C), 131.8 (C), 134.3 (C), 135.6 (C), 136.5 (C), 139.6 (C), 140.5 (C), 145.4 (C), 156.7 (C), 202.8 (C=O) ppm. HRMS calcd. for $C_{28}H_{42}O_2Si$ [MNa]: 461.2852; found 461.2850.

1-(4-{3-[2-(*tert*-Butyldimethylsilyl)-1-methylvinyl]-4-methylpent-3-[lxenyl}-1,2,5,7-tetrahydro-6-oxacyclobuta[*e*]inden-3-yl)propenone (37): NaHMDS (2 M solution in THF, 0.5 mL, 0.95 mmol) was added dropwise to a cooled (–40 °C) solution of **36** (320 mg 0.73 mmol) in THF (8 mL). The solution was stirred at this temperature for 1 h and then phenylselenyl chloride (209 mg, 1.09 mmol) was added. The mixture was warmed up to room temperature and stirred until completion of the reaction (TLC). The reaction mixture was extracted with Et_2O, washed with water and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was used without further purification in the next step. $NaHCO_3$ (92 mg, 1.09 mmol) and $NaIO_4$ (312 mg, 1.46 mmol) were added to a solution of the preceding compound in MeOH (12 mL)/H_2O (1.95 mL)/CH_2Cl_2 (1.5 mL). The mixture was stirred until completion of the reaction (TLC). The solution was diluted with Et_2O, washed with water and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was purified by flash chromatography to give compound **37** (202 mg, 63% over 2 steps) as a yellow oil. IR (ATR): $\tilde{\nu}$ = 2925, 2853, 1668, 1607, 1246, 822, 759 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 21 °C): δ = 0.00 [s, 6 H, Si(CH_3)$_2$*t*Bu], 0.79 [s, 9 H, SiC(CH_3)$_3$Me$_2$], 1.51 [s, 3 H, =C(CH_3)$_2$], 1.59 [s, 3 H, =C(CH_3)$_2$], 1.70 [s, 3 H, =C(CH_3)], 2.12 (m, 2 H, CH_2–CH_2), 2.40 (m, 2 H, CH_2–CH_2), 3.00 [m, 2 H, CH_2(cyclobutene)], 3.13 [m, 2 H, CH_2(cyclobutene)], 4.92 (br. s, 4 H, CH_2–O–CH_2), 4.97 (s, 1 H, Si–CH=), 5.83 (dd, J = 10.6, 1.6 Hz, 1 H, H_2C=CH), 6.08 (dd, J = 17.5, 1.6 Hz, 1 H, H_2C=CH), 6.62 (dd, J = 17.4, 10.6 Hz, 1 H, H_2C=CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 21 °C): δ = –3.8 (2 CH_3), 17.7 (C), 19.8 (CH_3), 22.1 (CH_3) 22.3 (CH_3), 26.9 (3 CH_3), 28.7 (CH_2), 30.8 (CH_2), 31.7 (CH_2), 32.8 (CH_2), 72.4 (CH_2O–), 73.1 (CH_2O–), 124.5 (C), 125.1 (CH), 130.9 (CH_2), 132.1 (C), 135.2 (C), 136.0 (C), 136.5 (C), 137.5 (CH), 139.5 (C), 140.6 (C), 145.3 (C), 156.8 (C), 194.7 (C=O) ppm. HRMS calcd. for $C_{28}H_{40}O_2Si$ [MNa]: 459.2675; found 461.2695.

Compound 38: $Et_2O{\cdot}BF_3$ (48% in Et_2O, 0.18 mL, 0.69 mmol) was added to a cooled (–50 °C) solution of **37** (60 mg, 0.14 mmol) in $CHCl_3$ (10 mL). The mixture was stirred until completion of the reaction (TLC). The solution was diluted with Et_2O, washed with $NaHCO_3$ solution and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude oil was purified by flash chromatography to give compound **38** (29 mg, 65%) as a white solid. IR (ATR): $\tilde{\nu}$ = 744, 898, 1054, 1456, 1672, 2923 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 21 °C): δ = 0.70 [s, 3 H, (CH*$_3$)C=C], 1.18 (s, 3 H, CH*$_3$), 1.24 (s, 3 H, CH*$_3$), 1.58 (m, 2 H, =C–CH_2–CH_2), 1.99 (m, 2 H, =C–CH_2–CH_2), 2.24 (m, 2 H, CH_2–CH_2), 2.46 (m, 2 H, CH_2–CH_2–), 2.58 [d, J = 7.1 Hz, 1 H, –CH–C(O)], 3.01 [m, 4 H, CH_2(cyclobutene)], 4.90 (s, 2 H, CH_2–O), 4.97 (m, 2 H, CH_2–O) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 21 °C): δ = 19.3 (CH_3), 23.8 (CH_3), 23.8 (CH_2), 26.5 (CH_2), 26.8 (CH_2), 27.3 (CH_2), 27.4 (CH_3), 28.7 (C), 28.9 (CH_2), 29.5 (CH_2), 61.8 (CH), 70.9 (CH_2–O), 71.7 (CH_2–O), 126.3 (C), 130.8 (C), 131.1 (C), 132.3 (C), 134.5 (C), 136.9 (C), 138.2 (C), 138.3 (C), 213.3 (C=O). HRMS calcd. for $C_{22}H_{26}O_2$ [MNa]: 345.1830; found 345.1855.

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