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Palladium-Catalyzed Oligocyclizations of 2-Bromoalk-1-ene-(*n*+1),(*m*+*n*+1)-diynes – Influence of Tether Lengths and Substituents on the Outcome of the Reaction (Part I)

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The outcomes and the mechanistic pathways of the palladium-catalyzed Heck-type cascade oligocyclizations of various 2-bromoalkenediynes were explored with respect to the lengths of the tethers between the multiple bonds and the nature of the substituent at the acetylenic terminus. Just like substrates containing two three-atom tethers, 2-bromotridec-1-ene-6,13-diynes **10a**,**b** with one three- and one four-atom tether undergo two consecutive intramolecular 5- and 6-*exo-dig* carbopalladations with subsequent 6π-electrocyclization and β-hydride elimination to form tricycles **35a**,**b** with a central benzene ring in 67 and 61 % yield, respectively, independent of the fact that **10a** contains an electron donor and **10b** an electron acceptor at the acetylene terminus. However, when 2-bromotetradec-1-ene-7,13-diynes **22**, **29** on one side and **16**, **27**, **31** on the other are subjected to Heck reaction conditions, tricycles with a central benzene ring are formed only, when the substituent at the acetylene terminus is not a methoxycarbonyl group as in **22**, **29**. Thus, the bisannelated benzene derivatives **36** and **37** are formed from **22** and **29** in 79 and 18 % yield, respectively, whereas **16**, **27** and **31** with their methoxycarbonyl substituents at the acetylenic end yield tetracyclic systems **38**, **39** and **40**, consisting of a central five-membered and two annelated six-membered as well as an additional annelated three-membered ring, predominantly (54, 19 and 18 % yield, respectively). The cascade reaction leading to the latter products must involve a 5-*exo-trig* carbopalladation rather than 6π-electrocyclization as the third step. Apparently, the nature and the substitution pattern of the tether in the substrates **16**, **22**, **31** linking the vinyl bromide moiety with the internal acetylene affect the yield of the tetracyclic product.

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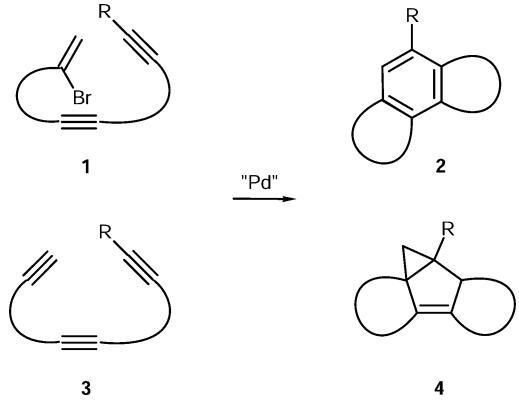
Introduction

The formation of new carbon–carbon bonds is one of the primary goals in synthetic organic chemistry. With the advent of modern synthetic methodologies, such bonds can be constructed with high chemo-, regio-, and stereoselectivities. In this regard, organometallic chemistry has provided a myriad of valuable methods which can be considered a field by their own. Thus, the variety of modern metal-catalyzed cross-coupling reactions[1] have significantly facilitated the efficient assembly of many complex organic frameworks as present in natural and non-natural biologically active compounds. Further advances can be achieved by making more than one carbon–carbon bond in a one-pot reaction or at least in a single operation.[2] Such domino processes or cascade reactions[3] are providing efficient and economical methods for the construction of complex skeletons. The development of such cascades to access oligocyclic structures from open-chain precursors has also been under thorough investigation in our[4] as well as other groups[5] during the last two decades.

In utilizing different types of palladium-catalyzed processes (Heck reactions,[6] cycloisomerizations[7]) to effect such oligocyclizations, many investigations were concerned



Scheme 1. Intramolecular palladium-catalyzed oligocyclization cascades of bromo-enediynes and triynes.

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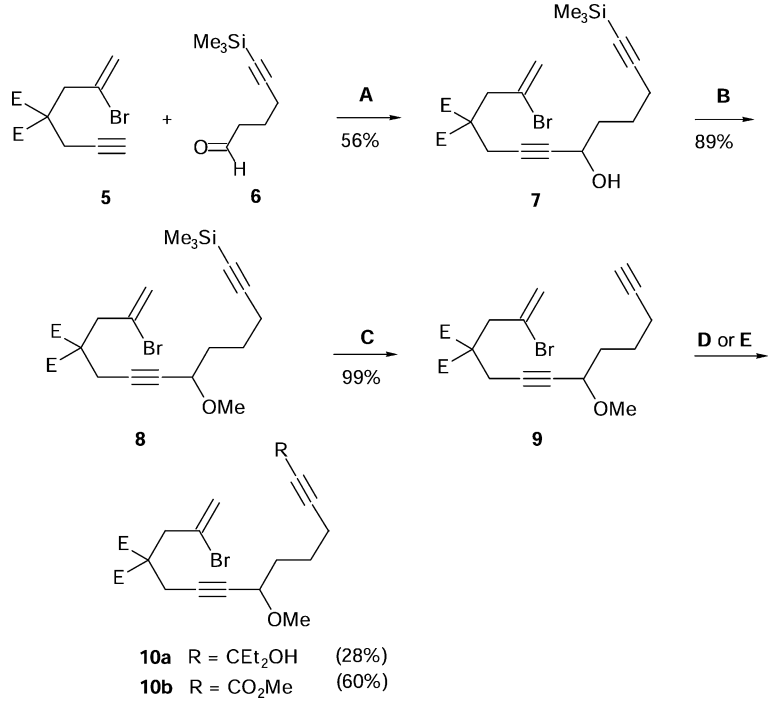
with the outcomes of these cascades and exploring the mechanistic pathways leading to the observed products. However, the factors which determine these pathways and hence control the outcome selectivity of these cascades have not been determined. Therefore, we have set out to investigate the effect of the tether lengths and nature of the terminal substituents in 2-bromoalk-1-ene-(*n*+1),(*m*+*n*+1)-diynes on determining the mechanistic pathways of their oligocyclizations (Scheme 1).[8]

Results and Discussion

Preparation of the Oligocyclization Substrates

The synthesis of the two 2-bromotridec-1-ene-6,12-diynes **10a**,**b** with three- and four-atom tethers, respectively, between the C,C-multiple bonds started with the previously described diethyl malonate derivative **5**[9] containing a 2-bromohept-1-en-6-yne unit. The latter was deprotonated at the acetylene terminus with *n*-butyllithium, and the resulting lithium acetylide was treated with 6-(trimethylsilyl)-hex-5-ynal (**6**), prepared according to a method reported by Stetter et al.[10] to afford the propargyl alcohol derivative **7** in 56% yield (Scheme 2). The hydroxy group in **7** was methylated by deprotonation with *n*-butyllithium and subsequent treatment with methyl iodide to give **8**, the terminal acetylene of which was desilylated with silver nitrate in aqueous ethanol to yield **9** (99%). The terminal acetylene in **9** was then functionalized by deprotonation with *n*-butyllithium in THF at –78 °C and ensuing treatment with diethyl ketone or methyl chloroformate to furnish the desired substrates **10a** and **10b** with 2-bromotridec-1-ene-6,12-diyne skeletons in 28 and 60% yield, respectively.

The synthesis of an analogous oligocyclization substrate **16**, in which the unsaturated moieties are linked by two four-atom tethers started with 1,7-octadiyne (**11**), prepared according to a literature procedure by twofold substitution of 1,4-diiodobutane with sodium acetylide.[11] Monodeprotonation of **11** with one equivalent of *n*-butyllithium and addition of the resulting acetylide to ethylene oxide activated by boron trifluoride diethyl etherate afforded deca-3,4-diyn-1-ol (**12**) in 55% yield (Scheme 3). Clearly, the moderate yield of this reaction must be attributed to the presence of two terminal acetylene units in **11**. Furthermore, the reaction was quenched with water at –78 °C to avoid subsequent side reactions, and this probably was not completely efficient. The alcohol **12** was converted into the corresponding mesylate **13** which was used to alkylate sodium dimethyl malonate enolate to give **14** (72%).[12] The sodium enolate of the latter was then allylated with 2,3-dibromopropene in dimethoxyethane (DME) at 70 °C to provide **15** in very poor yield. The yield could be raised to 75% by adding a small fraction (10–15% by volume) of dimethylformamide (DMF) to the DME. The final step, the attachment of the methoxycarbonyl group to the alkyne terminus of **15**, was achieved by deprotonation with lithium diisopropylamide (LDA) at –78 °C and subsequent reaction with methyl chloroformate to give the desired 2-bromotetradec-1-ene-7,13-diyne derivative **16** (45% yield).



Scheme 2. Synthesis of 2-bromotridec-1-ene-6,12-diyne derivatives containing a three- and a four-atom tether between the C,C-multiple bonds; **A**: 1) *n*BuLi, –78 °C, THF, 2) aldehyde **6**, –78→0 °C; **B**: 1) *n*BuLi, –78 °C, THF, 2) MeI, DMSO, 25 °C, 2 h; **C**: 1) $AgNO_3$, EtOH/H_2O, 2) KCN, 25 °C, 4 h; **D**: *n*BuLi, –78 °C, THF, $ClCO_2Me$; **E**: *n*BuLi, –78 °C, THF, Et_2CO. E = CO_2Et.

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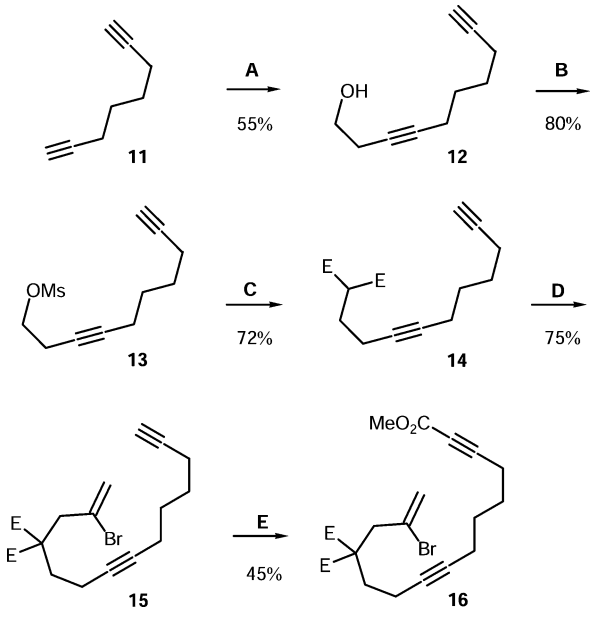
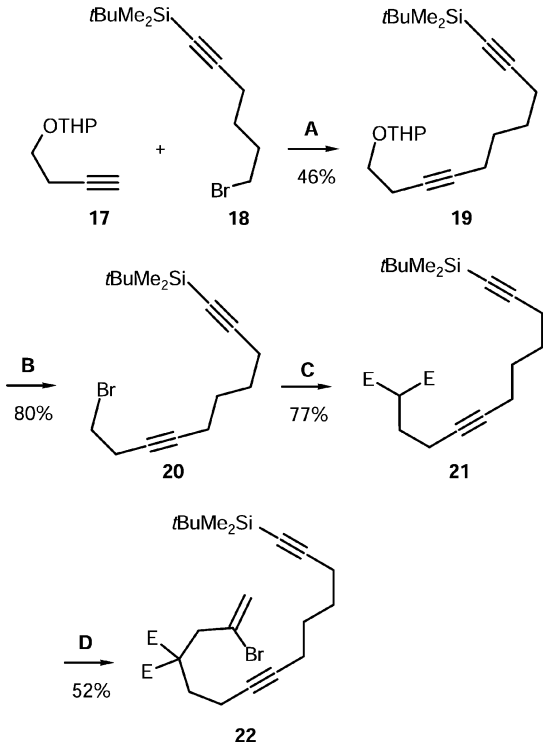
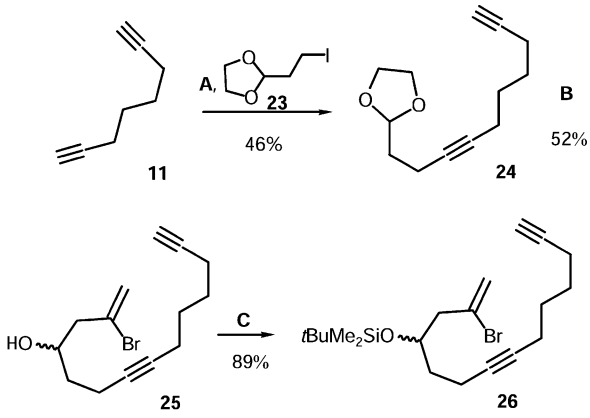


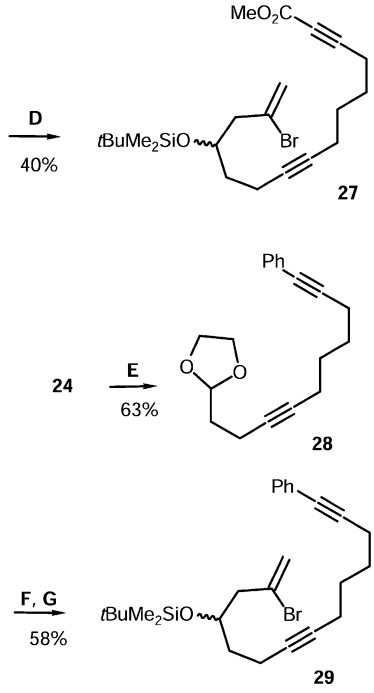
Scheme 3. Synthesis of a methoxycarbonyl-terminated 2-bromotetradec-1-ene-7,13-diyne with two four-atom tethers between the multiple bonds: **A**: 1) *n*BuLi, –78 °C, THF, 2) BF_3·Et_2O, ethylene oxide, –78 °C, 2 h; **B**: Et_3N, MsCl, CH_2Cl_2 –15→0 °C, 12 h; **C**: NaH, dimethyl malonate, KI, THF/DMF, 18 h, 70 °C; **D**: NaH, 2,3-dibromopropene, DME/DMF, 20 h, 70 °C; **E**: LDA, $ClCO_2Me$, THF, –78 °C, 1 h, room temp., 2 h. E = CO_2Me.



Scheme 4. Synthesis of a *tert*-butyldimethylsilyl-terminated 2-bromotetradec-1-ene-7,13-diyne. **A**: 1) *n*BuLi, THF, –78 °C, 30 min, 2) HMPA, **18**, room temp., 5 h; **B**: PPh_3, Br_2, CH_2Cl_2, 30 min, –15 °C, room temp., 20 h; **C**: NaH, dimethyl malonate, DMF, 36 h, **D**: NaH, 2,3-dibromopropene, DME, 4 h, 70 °C. E = CO_2Me.

An analogous 2-bromotetradec-1-ene-7,13-diyne **22** with a *tert*-butyldimethylsilyl group at the alkyne terminus was prepared by deprotonating 2-(3′-butynyloxy)tetrahydro-2*H*-pyran (**17**) with *n*-butyllithium and treating the resulting lithium acetylide with 6-bromo-1-(*tert*-butyldimethylsilyl)-hexyne (**18**) to afford 2-(10′-(*tert*-butyldimethylsilyl)deca-3′,9′-diynyloxy)tetrahydro-2*H*-pyran (**19**) in 46% yield. According to a reported procedure,[13] treating **19** at –20 °C with triphenylphosphane and bromine in dichloromethane directly converted the tetrahydropyranyloxy group of **19** into a bromine substituent and afforded 10-bromo-1-(*tert*-





Scheme 5. Syntheses of 2-bromotetradec-1-ene-7,13-diynes **23**, **25** without a malonate moiety in the tether linking the vinyl bromide to the internal acetylene fragment; **A**: *n*BuLi, THF, **17**, HMPA, –78 °C→r.t.; **B**: Sn, HBr (48%), Et_2O/H_2O (5:2), 2,3-dibromopropene, room temp.; **C**: imidazole, *t*$BuMe_2SiCl$, DMF, 55 °C, 24 h; **D**: LDA, $ClCO_2Me$, THF, –78 °C, 1 h, room temp., 2 h. **E**: $PdCl_2(PPh_3)_2$ (0.5 mol-%), CuI (1 mol-%), PPh_3 (2 mol-%), Et_3N, iodobenzene, 40 °C, 14 h; **F**: Sn, HBr (48%), Et_2O/H_2O (5:2), 2,3-dibromopropene, room temp., 5 d; **G**: imidazole, *t*$BuMe_2SiCl$, DMF, 55 °C, 24 h.

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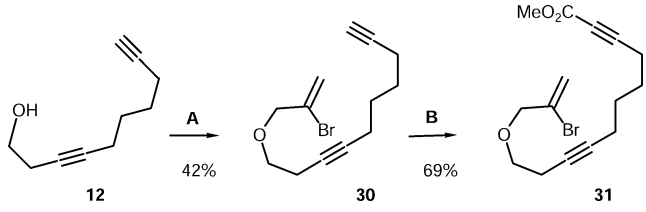
butyldimethylsilyl)-deca-3,9-diyne (**20**) in 80% yield. The produced bromodiyne (**20**) was used to alkylate sodium dimethyl malonate enolate to produce **21** in 77% yield. The sodium enolate of **21** was allylated with 2,3-dibromopropene to furnish the desired precursor **22** in 52% yield (Scheme 4).

Three more oligocyclization substrates with two four-atom tethers between the multiple bonds, but without a malonate moiety in the tether linking the vinyl bromide to the internal acetylene fragment, were prepared. One of these syntheses started with the alkylation of the monolithiated 1,7-octadiyne with the dioxolane-protected 3-iodopropanal **23**[14] to give **24** in 46% yield (Scheme 5). The acetal-protected aldehyde **24** was then directly coupled to 2,3-dibromopropene employing tin powder[15] to give the alcohol **25** in 52% yield, and the hydroxy group in **25** was protected as the *tert*-butyldimethylsilyl ether **26** (89% yield). Finally, a methoxycarbonyl group was installed at the terminal alkyne employing the same method as for **16** to give the analogous substrate **27** (40% yield).

Sonogashira coupling of the terminal acetylene of **24** with iodobenzene provided the phenyl-substituted diyne **28** with the protected aldehyde terminus, from which the 2-bromo-14-phenyltetradec-1-ene-7,13-diyne **29** was obtained in 57% yield by tin-mediated coupling with 2,3-dibromopropene and protecting the resulting hydroxy group as a *tert*-butyldimethylsilyl ether (Scheme 5).

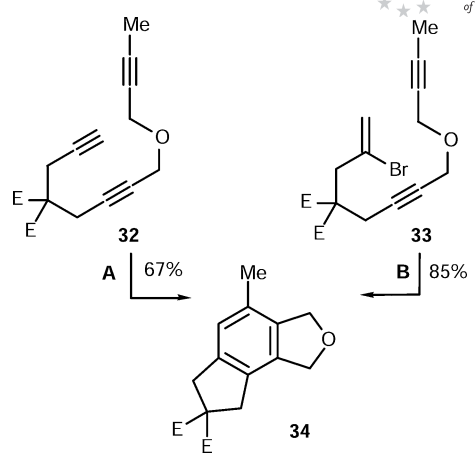
Allylation of the deca-3,9-diyn-1-ol (**12**) with 2,3-dibromopropene gave the oxygen-linked bromodiyne **30** to which a methoxycarbonyl group could be attached at the alkyne terminus to provide **31** (Scheme 6).



Scheme 6. Synthesis of a 2-bromotetradec-1-ene-7,13-diyne with an oxygen in the tether between the vinyl bromide and the internal alkyne moiety; **A**: NaH, 2,3-dibromopropene, THF, 60 °C; **B**: LDA, $ClCO_2Me$, THF, –78 °C, 1 h, room temp., 2 h.

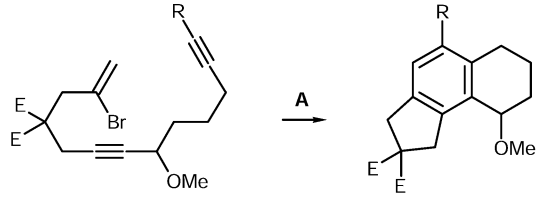
Palladium-Catalyzed Oligocyclizations

In an earlier study, Negishi et al.[16] disclosed palladium-catalyzed intramolecular cascade reactions of a triyne like **32** and a bromo-enediyne like **33** in which the three multiple bond fragments were linked by two three-atom tethers, giving rise to tricyclic skeletons, like **34**, with two five-membered rings annelated to a central six-membered aromatic ring (Scheme 7). The same type of bisannelated benzene derivatives were formed, when 2-bromotridec-1-ene-6,12-diynes and 2-bromotridec-7,12-diynes, i.e. 2-bromoalkene-diynes with one three- and one four-atom tether between the multiple bonds, were subjected to typical Heck reaction conditions [e.g. $Pd(OAc)_2$, Ph_3P, K_2CO_3, MeCN].[8a]



Scheme 7. Palladium-catalyzed tricyclization of a dodeca-1,6,11-triyne and a 2-bromododec-1-ene-6,11-diyne containing two three-atom tethers according to Negishi et al.[16] **A**: $Pd(PPh_3)_4$ (3 mol-%), HOAc (5 mol-%), MeCN, reflux, 12 h; **B**: $Pd(PPh_3)_4$ (3 mol-%), Et_3N (2 equiv.), MeCN, reflux, 12 h. E = CO_2Et.

Thus, when the 2-bromotridec-1-ene-6,12-diynes **10a**,**b** in acetonitrile were treated with palladium acetate (5 mol-%) in the presence of triphenylphosphane (20 mol-%) and potassium carbonate (2 equiv.) at 120 °C for 2–3 h, the bisannellated benzene derivatives **35a**,**b** were obtained in 67 and 61% yield, respectively (Scheme 8).



Scheme 8. Palladium-catalyzed tricyclization of 2-bromotridec-1-ene-6,12-diynes containing one three- and one four-atom tether. **A**: $Pd(OAc)_2$ (5 mol-%), PPh_3 (20 mol-%), K_2CO_3 (2 equiv.), MeCN, 120 °C. E = CO_2Et.

The formation of the aromatic compounds was easily detected by the appearance of a singlet signal in the range 7.30–7.70 ppm and the disappearance of the signals of the vinylic protons in the ^1H NMR spectra. This was further confirmed by the disappearance of the acetylenic carbon signals and the appearance of six new signals each in the region of aromatic carbon signals in the ^{13}C NMR spectra.

Apparently, the outcome of these tricyclizations is not affected by the nature of the substituent at the acetylenic terminus, be it an electron-donating group as in **10a** or an electron-withdrawing group as in **10b**.

On the other hand, open-chain enediynes containing two four-atom tethers which, by the same reaction mode, would lead to tricyclic systems consisting of six-membered rings only, turned out to be highly sensitive to the nature of the substituent at the acetylene terminus. Thus, when the acetylene terminus in such an enediyne was substituted with a *tert*-butyldimethylsilyl or a phenyl group as in **22** and **29**,

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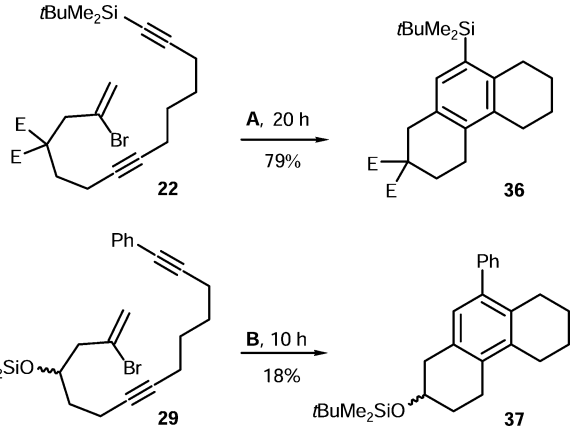
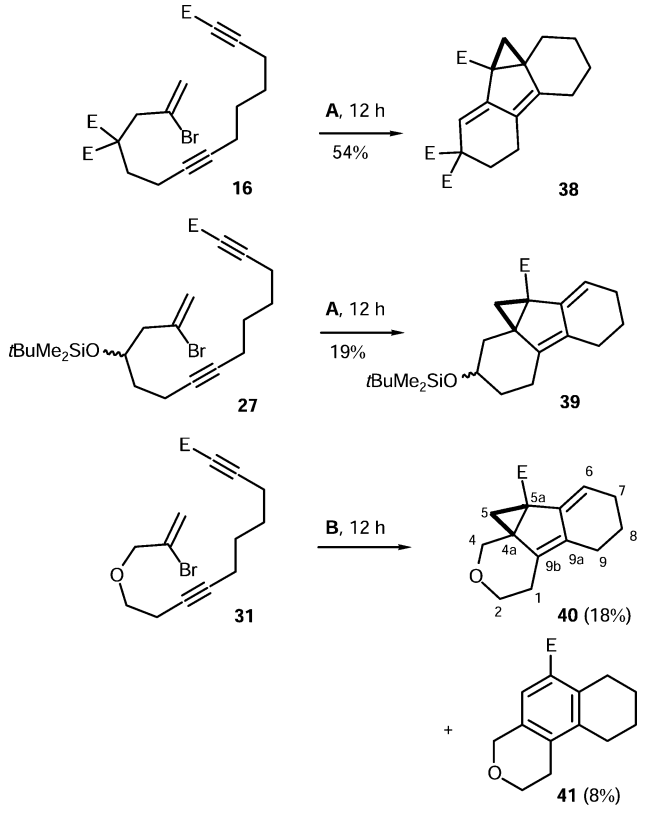
respectively, treatment with typical Heck precatalyst systems produced octahydrophenanthrene derivatives **36** and **37** with a central benzene ring in 79 and 18% yield, respectively (Scheme 9).

Surprisingly, all of the 2-bromotetradec-1-ene-7,13-diynes **16**, **27**, **31** with electron-withdrawing methoxycarbonyl groups at the acetylene terminus, upon treatment with a palladium precatalyst mixture (10 mol-% of $PdOAc_2$, 25 mol-% of PPh_3, and 3 equiv. of K_2CO_3) in acetonitrile at 60 °C (for **16** and **27**), and 110 °C (for **31**), respectively, gave the tetracyclic systems, **38**, **39** and **40**, respectively, each containing a cyclopropyl moiety (Scheme 10). Apparently, these cascade cyclizations proceed along routes that are different from those for all of the other bromo-enediynes presented above.

The tetracyclic structures of these products were assigned on the basis of their ^1H and ^{13}C NMR spectra and additional 2D-NMR experiments. The disappearance of the signals of the acetylenic carbons and the appearance of four new signals of olefinic carbons in each of the ^{13}C NMR spectra indicated the formation of two new double bonds. DEPT (135°) and APT measurements indicated that one of them is tetrasubstituted, while the other is trisubstituted. The ^1H NMR spectra each show a signal in the olefinic region (δ = 5.90–6.10 ppm) which corresponds to an olefinic proton. They also show the appearance of two unique doublets in the regions (δ = 1.03–1.08 and 1.90–2.02 ppm, ^2J = 2.9–3.15 Hz) which correspond to the *exo*- and *endo*-protons of a ring-annelated cyclopropyl methylene group. According to 2D-NMR correlation, especially ^1H-^{13}C multiple bond correlation (HMBC) spectra, the positions of the diene and the cyclopropyl moieties could be assigned. The large NOE enhancement between the *exo*-proton of the cyclopropyl moiety and the equatorial α-proton in the pyran ring of **40** (Figure 1) provided further evidence for the presence and the position of the cyclopropyl moiety.



Scheme 9. Palladium-catalyzed tricyclizations of 2-bromotetradec-1-ene-7,11-diynes containing two four-atom tethers. **A**: $Pd(OAc)_2$ (10 mol-%), PPh_3 (25 mol-%), K_2CO_3 (3 equiv.), MeCN, 20 h, 60 °C; **B**: $Pd(OAc)_2$ (10 mol-%), PPh_3 (25 mol-%), HO_2CNa (1.5 equiv.), DMF, 10 h, 80 °C. E = CO_2Me.



Scheme 10. Palladium-catalyzed cascade cyclizations of 2-bromotetradec-1-ene-7,13-diynes containing two four-atom tethers and terminal electron-withdrawing groups. **A**: $Pd(OAc)_2$ (10 mol-%), PPh_3 (25 mol-%), K_2CO_3 (3 equiv.), MeCN, 60 °C; **B**: $Pd(OAc)_2$ (10 mol-%), PPh_3 (25 mol-%), K_2CO_3 (3 equiv.), MeCN, 110 °C. E = CO_2Me.

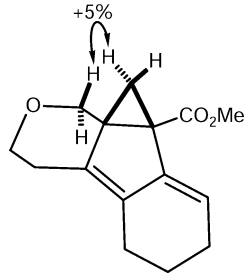


Figure 1. NOE enhancements in the NOE-NMR spectrum of the tetracyclic diene **40**.

It is noteworthy that the type of substitution on the tether linking the vinyl bromide moiety and the internal acetylene would mainly affect the yield.

Discussion

The differently proceeding cascade oligocyclizations of the various 2-bromoalk-1-ene-(n+1),(m+n+1)-diynes can be rationalized on the basis of previous observations (Scheme 11).

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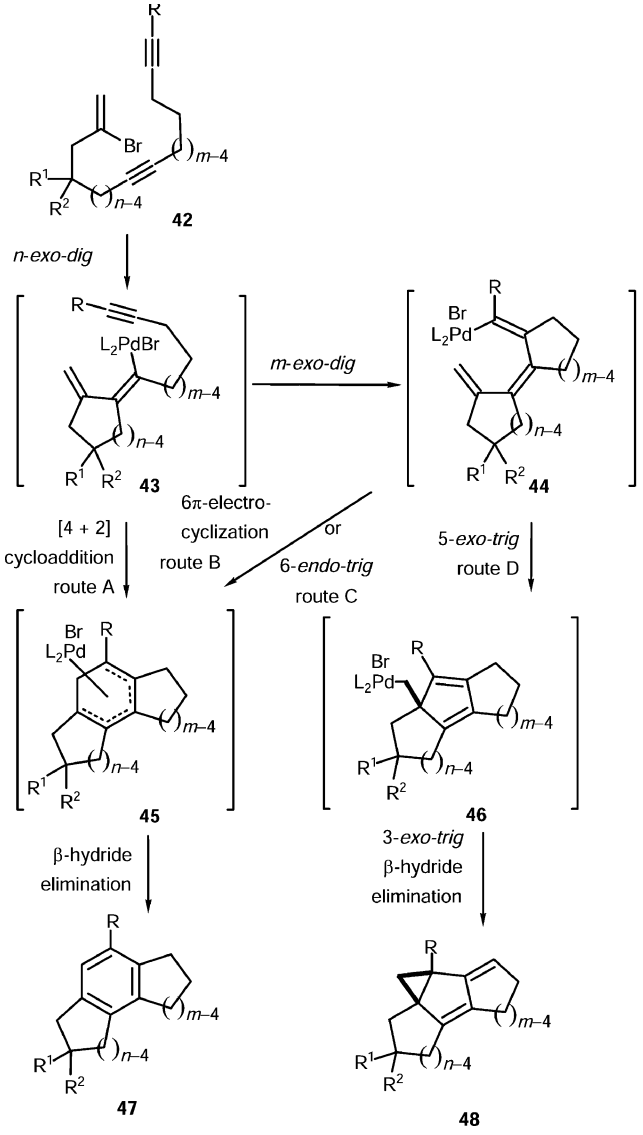

Scheme 11. Possible pathways for cascade oligocyclizations of 2-bromoalk-1-ene-(*n*+1),(*m*+*n*+1)-diynes **42**, *n* = 5 or 6, *m* = 5 or 6.

In any event, the reaction does start with an oxidative addition of the vinyl bromide moiety to the catalytically active, in situ formed palladium(0) species, and this is succeeded by an intramolecular *n-exo-dig* carbopalladation typical for an intramolecular Heck reaction to form the first ring. This might be followed by an intramlecular [4+2] cycloaddition to yield the cyclohexadienylpalladium species **45**, (route A) or by another *m-exo-dig* carbopalladation to form the 1,3,5-hexatrienylpalladium intermediate **44**. A third ring may result from either of three processes. Both a 6π-electrocyclization (route B) or a 6-*endo-trig* carbopalladation (route C) would also lead to **45**, while a 5-*exo-trig* carbopalladation to produce the neopentyl-type σ-alkylpalladium species **46** (route D) apparently becomes a favored option, when the preferred conformation of the square-planar hexa-1,3,5-trienyl-σ-palladium intermediate **44** puts the palladium in a suitable position to coordinate the *exo*-methylene group (see Figure 2). This situation arises when the two exomethylene groups in intermediate **44** are not in the same plane. Coplanar or nearly coplanar 1,3,5-hexatrienes prefer to undergo 6π-electrocyclization, as is observed for intermediates **44** (*n* = *m* = 5) comprising two five-membered rings (Figure 2, **A**).

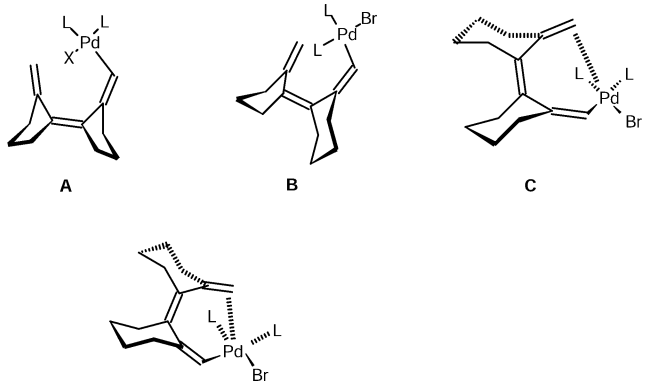

Figure 2. Optimized geometries of the hexa-1,3,5-trienylpalladium intermediate **44** varying with the sizes of the two incorporated rings.

Accordingly, the formation of the tricycle **34** from **33** and **32** most probably arises by 6π-electrocyclization of the intermediate of type **44** (*n* = *m* = 5) and subsequent β-hydride elimination from the intermediate **45**. Direct formation of **45** by an intramolecular [4+2] cycloaddition in **43** (route A in Scheme 11) is less likely, because the terminal triple bond in **32** and **33** is not particularly activated for such a cycloaddition, yet it cannot be excluded. These results are also in agreement with the findings of Trost et al.[17] In their study, they found that the palladium-catalyzed cycloisomerization of enediyne substrates comprising two three-atom tethers can occur by 6π-electrocyclization and by intramolecular Diels–Alder reaction.

A similar case arises when the intermediate **44** comprises one five- and one six-membered ring (*n* = 5, *m* = 6). In this case the geometry of the five-membered ring will dominate the resulting conformation of the intermediate **44**, which will not allow the square-planar σ-palladium complex to coordinate to the opposite exomethylene group precluding the possibility for the intermediate **44** to undergo yet another carbopalladation step (Figure 2, **B**).

This is further supported by the fact that the outcomes of the oligocyclization cascades of the substrates comprising one three- and one four-atom tether, such as **10**, are insensitive to the nature of the substituent at the terminal acetylene. Thus, only a single type of product, namely the tricyclic aromatic system **35**, was observed (Scheme 8). This apparently leaves 6π-electrocyclization as the only allowed option for the intermediate **44** (*n* = 5, *m* = 6). In addition, intramolecular [4+2] cycloaddition (route A, Scheme 11), cannot be considered an option for the oligocyclization cascades of these substrates. This is due to the length of the tether linking the diene to the dienophile.

On the other hand, when the intermediate **44** comprises two six-membered rings (*n* = *m* = 6), it will have enough flexibility to adopt a conformation which makes the two

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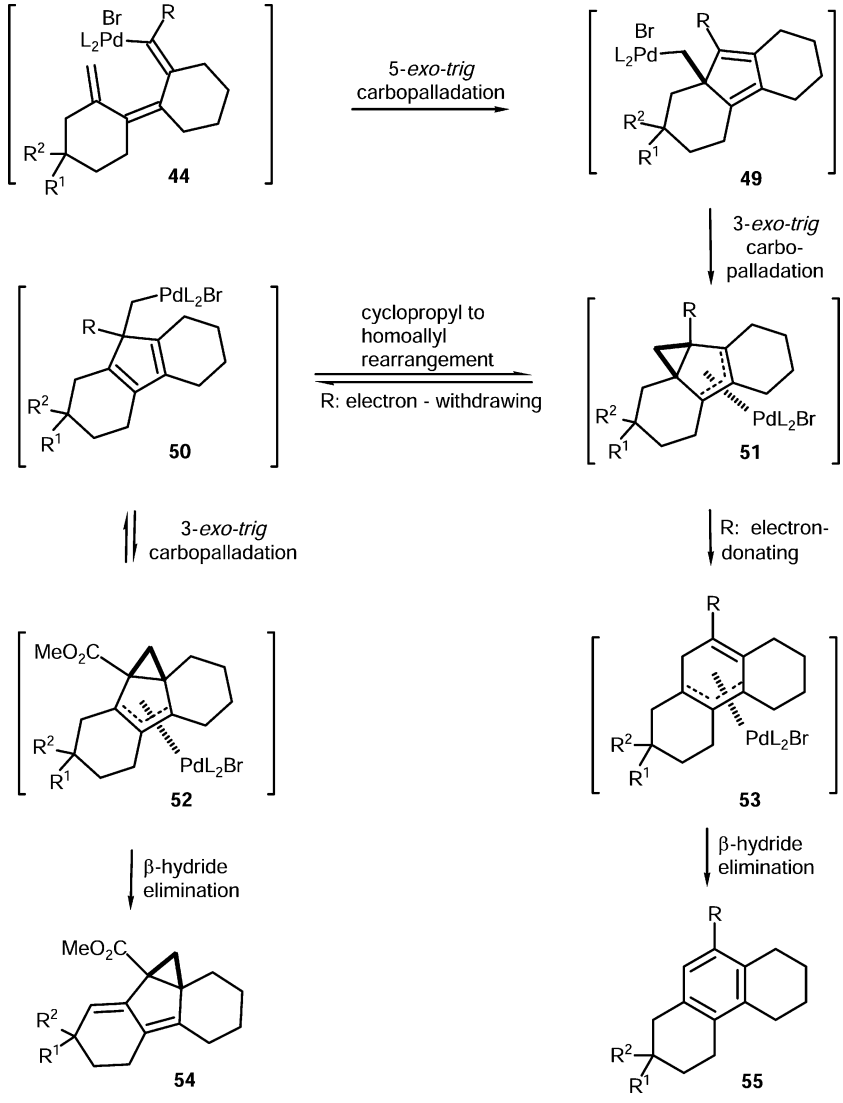
planes of the two exomethylene not coplanar to each other (Figure 2, **C**). This will put the square-planar σ-palladium complex in an appropriate position to coordinate the opposite exomethylene group (Figure 2). Therefore, carbopalladation will become a more favored pathway for this intermediate than 6π-electrocyclization.

The formation of the tetracyclic systems such as **38**, **39** and **40** supports this explanation. It also indicates that the intermediate **44** ($n = m = 6$) undergoes this carbopalladation step in a 5-*exo*-*trig* (route D, Scheme 11) and not in a 6-*endo*-*trig* (route C, Scheme 11) fashion. Furthermore, it shows that the oligocyclization cascades for the substrates containing two four-atom tethers cannot occur by an intramolecular [4+2] cycloaddition (route A, Scheme 11) or 6π-electrocyclization (route B, Scheme 11). After undergoing a 5-*exo*-*trig* carbopalladation step, the cascade continues by a series of 3-*exo*-*trig* carbopalladations and rearrangements before it terminates by β-hydride elimination.

The variety of the outcomes of the oligocyclization of these substrates is attributed to the substituent nature at the terminal acetylene. Scheme 12 illustrates the electronic effect of these substituents.

Thus, after the intermediate **44** has undergone a 5-*exo*-*trig* carbopalladation, the generated neopentyl-type system **49** will experience a 3-*exo*-*trig* carbopalladation to furnish **51**. Depending on the nature of the R group, **51** can undergo cyclopropyl to homoallyl rearrangement in two ways. The first version occurs when R is an electron-withdrawing group. In this way, **51** will experience cyclopropyl to homoallyl rearrangement by breaking the cyclopropyl bond which is not substituted with the R group to produce **50**. Subsequently, **50** will undergo a 3-*exo*-*trig* carbopalladation and β-hydride elimination to furnish the kinetically stable tetracyclic system **54**. The second version occurs, when R is an electron-donating group. In this case, **51** will experience cyclopropyl to homoallyl rearrangement by breaking the



Scheme 12. The effect of the substituent on the acetylene terminus on the route and outcome of the cascade oligocyclization of 2-bromotetradec-1-ene-7,13-diynes via 1,3,5-hexatrienylpalladium intermediate **44**.

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cyclopropyl bond which is substituted with the R group to produce **53**. The latter will undergo β-hydride elimination to produce the thermodynamically more stable bisanellated benzene system **55**.

Conclusions

Palladium-catalyzed cascade oligocyclizations of 2-bromoalkenediynes are valuable and economical methods to access complex organic skeletons. To be able to anticipate the outcome of such cascades requires an understanding of the factors which affect the reaction modes of these cascades. It is obvious from this study that the lengths of the tethers between the multiple bonds and the nature of the substituents at the terminal acetylene exert a significant effect on the outcomes and the yields of such oligocyclization cascades. 2-Bromotetradec-1-ene-7,13-diynes behave like 2-bromododec-1-ene-6,11-diynes and 2-bromotridec-6,12-diynes only, if they do not carry a methoxycarbonyl substituent at their acetylenic terminus. With such an electron-withdrawing group, the systems undergo tetracyclizations involving a 5-*exo*-*trig* carbopalladation rather than 6π-electrocyclization as the third step, which would be succeeded by a β-hydride elimination. It is not surprising that a *gem*-bis(methoxycarbonyl) substitution as in **16** favors the first cyclization step by its Thorpe–Ingold effect,[18] and thus leads to a higher yield of the tetracyclic product.

Experimental Section

General Remarks: ^{1}H NMR spectra were recorded with Bruker AM 250 (250 MHz), Varian INOVA-500 (500 MHz) and Varian INOVA-600 (600 MHz) instruments at ambient temperature in $CDCl_3$ or C_6D_6 with tetramethylsilane (δ = 0.00 ppm) as an internal standard. The line positions or centers of multiplets are given in ppm (δ) and the coupling constants (J) are reported as absolute values in Hertz [Hz]. Abbreviations for the signal multiplicities: s (singlet), br. s (broad singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), ddd (doublet of doublets of doublets), dt (doublet of triplets), tt (triplet of triplets), dq (doublet of quartets), tq (triplet of quartets), m (multiplet). Additional abbreviations: $J_{ax\text{-}ax}$ ($J_{axial\text{-}axial}$), $J_{ax\text{-}eq}$ ($J_{axial\text{-}equatorial}$), $J_{eq\text{-}eq}$ ($J_{equatorial\text{-}equatorial}$). ^{13}C NMR spectra were recorded with Bruker AM 250 (62.5 MHz), Varian INOVA-500 (125.7 MHz) and Varian INOVA-600 (150.8 MHz) instruments at ambient temperature in $CDCl_3$, with δ ($CDCl_3$) = 77.0 ppm as an internal standard. When signals could not be assigned unambiguously, the potentially corresponding atoms concerned are marked with an asterisk (*). The multiplicities of ^{13}C NMR signals were determined with the help of either DEPT (Distortionless Enhancement by Polarization Transfer) or APT (Attached Proton Test) measurements and are designated as follows: CH_3, CH = (+) (DEPT and APT), CH_2 = (–), (DEPT and APT), quaternary C = (–) (APT), (C_{quat}) (DEPT). Infrared spectra were recorded with a Bruker FT-IR spectrometer IFS 66. Mass spectra were recorded with Finnigan MAT CH 7 and MAT 731 spectrometers using electron impact ionization at 70 eV or direct chemical ionization with NH_3 as reactant gas. High-resolution mass spectra (HRMS) were recorded with a Finnigan MAT 311 or an INCOS 50 with Varian 34000 (GC-MS) instrument using preselected ion peak matching at $R \approx 10000$ to be within ± 2 ppm. Microanalysis: Mikroanalytisches Laboratorium des Instituts für Organische und Biomolekulare Chemie der Georg-August-Universität Göttingen. Column chromatography: Merck Kieselgel 60 (0.063–0.200 mm). Thick-layer chromatography; Merck Kieselgel PF_{254} containing $CaSO_4$. Thin-layer chromatography: Macherey–Nagel Alugram G/UV_{254} 0.25 mm silica gel with fluorescent indicator. Developer: molybdenumphosphoric acid solution (10% in ethanol). All operations were performed under a nitrogen or an argon atmosphere. Solvents were purified and dried according to conventional methods. The following abbreviations are used: DME = 1,2-dimethoxyethane, HMPA = hexamethylphosphortriamide, DMF = dimethylformamide, PE = light petroleum, boiling range 40–50 °C.

General Procedure for Palladium-Catalyzed Oligocyclizations of 2-Bromoalk-1-ene-(*n* + 1),(*m* + *n* + 1)-diynes Initiated by a Heck-Type Reaction (GP)

Method A: Palladium acetate (0.1 equiv.) is added at 60 °C to a degassed mixture, placed in a Pyrex® bottle with a screw cap, of triphenylphosphane (0.25 equiv.), potassium carbonate (2.5 equiv.), and the respective 2-bromoalk-1-enediyne (1 equiv.) in acetonitrile. After stirring at 60 °C for 1 to 12 h, the reaction mixture is cooled to room temperature, filtered through a layer each of Celite® and of charcoal, then concentrated. The residue is purified by either column chromatography or thick-layer chromatography (TLC) using 20 × 20 cm plates coated with silica gel 60 PF_{254} containing 2.5% $CaSO_4$.

Method B: Palladium acetate (0.1 equiv.) is added at 80 °C to a degassed mixture, placed in a Pyrex® bottle with a screw cap, of triphenylphosphane (0.25 equiv.), sodium formate (1.2 equiv.), and the respective 2-bromoalk-1-enediyene precursor (1 equiv.) in DMF. After stirring at 80 °C from 1 to 12 h, the reaction mixture is poured into water (30 mL) and extracted with diethyl ether (3 × 20 mL). The combined ether layers are dried ($MgSO_4$), concentrated and the residue is purified by either column chromatography or thick-layer chromatography (TLC) using 20 × 20 cm plates coated with silica gel 60 PF_{254} containing 2.5% $CaSO_4$.

Diethyl 2-Bromo-8-hydroxy-13-(trimethylsilyl)-1-tridecene-6,12-diyne-4,4-dicarboxylate (7): To a solution of dimethyl 2-(2-bromoallyl)-2-(2-propynyl)malonate[9] (**5**) (3 g, 9.5 mmol) in THF (20 mL) was added dropwise, at –78 °C, *n*-butyllithium (4.41 mL, 10.5 mmol, 2.4 M in hexane). After stirring at this temperature for 30 min, 6-(trimethylsilyl)hex-5-ynal (**6**) (1.59 g, 9.4 mmol) was added dropwise, and the reaction mixture was warmed to 0 °C. Water (20 mL) was added to the mixture, and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (90 g of flash silica gel, column 2 × 35 cm, PE/Et_2O, 1:1) to afford 2.7 g (60%) of **7** as a colorless oil, R_f (PE/Et_2O, 1:1) = 0.30. IR (film): $\tilde{\nu}$ = 3450 (OH), 2950, 2180 (C≡C), 1720 (C=O), 1630 (C=C), 1430, 1290, 1250, 1195, 920, 845, 760 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.08 [s, 9 H, $Si(CH_3)_3$], 1.24 (t, ^3J = 7.1 Hz, 6 H, CH_2CH_3), 1.58–1.77 (m, 4 H, 9- and 10-H), 2.23 (t, ^3J = 6.4 Hz, 3 H, 11-H and OH), 2.91 (d, ^5J = 1.9 Hz, 2 H, 5-H), 3.23 (s, 2 H, 3-H), 4.18 (m, 4 H, OCH_2CH_3), 4.32 (t, ^3J = 6.3 Hz, 1 H, 8-H), 5.58 (br. s, 1 H, 1-H), 5.78 (br. s, 1 H, 1-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 0.01 [+, $Si(CH_3)_3$], 13.9 (+, CH_2CH_3), 19.5 (–, C-11), 22.4 (–, C-5), 24.2 (–, C-10), 36.9 (–, C-9), 42.7 (–), 56.2 (C_{quat}, C-4), 61.9 (+, C-8), 61.9 (–, OCH_2CH_3), 79.7 (C_{quat}, C-7), 84.9 (C_{quat}, C-13), 106.7 (C_{quat}, C-12), 122.5 (–, C-1), 126.4 (C_{quat}, C-2), 169.0 (C_{quat}, 2 *C*OOEt) ppm.

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Diethyl 2-Bromo-8-methoxy-13-(trimethylsilyl)-1-tridecene-6,12-diyne-4,4-dicarboxylate (8): To a solution of **7** (4.57 g, 9.5 mmol) in THF (40 mL), kept at –78 °C, was added dropwise *n*-butyllithium (4.41 mL, 10.5 mmol, 2.4 M in hexane). After warming to 0 °C, a solution of methyl iodide (2.8 g, 19.9 mmol) in anhydrous DMSO (20 mL) was added, and stirring was continued at ambient temperature for 2 h. Water (20 mL) was added to the reaction mixture, and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (50 g of flash silica gel, column 2.5 × 35 cm, PE/Et_2O, 8:1) to afford 4.19 g (89%) of **8** as colorless oil, R_f (PE/Et_2O, 1:1) = 0.58. IR (film): $\tilde{\nu}$ = 2950, 2190 (C≡C), 1745 (C=O), 1630 (C=C), 1435, 1390, 1195, 850, 770, 705, 650 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.09 [s, 9 H, $Si(CH_3)_3$], 1.22 (t, ^3J = 7.2 Hz, 6 H, CH_2CH_3), 1.55–1.81 (m, 4 H, 9,10-H), 2.19 (t, ^3J = 7.0 Hz, 2 H, 11-H), 2.92 (d, ^2J = 1.8 Hz, 2 H, 5-H), 3.23 (s, 2 H, 3-H), 3.29 (s, 3 H, OCH_3), 3.88 (tt, ^5J = 1.8, ^3J = 6.4 Hz, 1 H, 8-H), 4.8 (m, 4 H, OCH_2CH_3), 5.56 (br. s, 1 H, 1-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 0.01 [+, $Si(CH_3)_3$], 13.9 (+, CH_2CH_3), 19.5 (–, C-11), 22.4 (–, C-5), 24.2 (–, C-10),34.7 (–, C-9), 42.8 (–, C-3), 56.1 (C_{quat}, C-4), 56.1 (+, OCH_3), 61.8 (–, OCH_2CH_3), 70.7 (+, C-8), 71.9 (C_{quat}, C-6), 80.6 (C_{quat}, C-7), 82.5 (C_{quat}, C-13), 106.7 (C_{quat}, C-12), 122.3 (–, C-1), 126.6 (C_{quat}, C-2), 168.9 (C_{quat}, 2 *C*OOEt) ppm.

Diethyl 2-Bromo-8-methoxy-1-tridecene-6,12-diyne-4,4-dicarboxylate (9): A solution of **8** (1.45 g, 2.9 mmol) in ethanol (3 mL) was added slowly to a solution of silver nitrate (658 mg,3.9 mmol) in ethanol (5 mL) and water (1.6 mL), upon which a precipitate formed immediately. After stirring at ambient temperature for 15 min, a solution of potassium cyanide (1.24 g, 19 mmol) in water (2.7 mL) was added, upon which most of the precipitate dissolved again. After stirring for 4 h at ambient temperature, water (50 mL) was added, and the reaction mixture was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (50 g of flash silica gel, column 2.5 × 20 cm, PE/Et_2O, 12:1) to afford 1.21 g (98%) of **9** as a colorless oil, R_f (PE/Et_2O, 2:1) = 0.37. IR (film): $\tilde{\nu}$ = 3300 (C≡CH), 2950, 2130 (C≡C), 1740 (C=O), 1640 (C=C), 1450, 1375, 1200, 910, 855, 640 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, ^3J = 7.1 Hz, 6 H, CH_2CH_3), 1.65 (m, 2 H), 1.73–1.83 (m, 2 H), 1.94 (t, ^4J = 2.6 Hz, 1 H, 13-H), 2.21 (dt, ^4J = 2.6, ^3J = 6.6 Hz, 2 H, 11-H), 2.98 (d, ^5J = 1.3 Hz, 2 H, 5-H), 3.29 (s, 2 H, 3-H), 3.34 (s, 3 H, OCH_3), 3.93 (t, ^3J = 6.3 Hz, 1 H, 8-H), 4.19 (m, 4 H, OCH_2CH_3), 5.61 (d, ^2J = 1.5 Hz, 1 H, 1-H), 5.79 (br. s, 1 H, 1-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.9 (+, CH_2CH_3), 18.1 (–, C-11), 22.5 (–, C-5), 24.2 (–, C-10), 34.7 (–, C-9), 42.8 (–, C-3), 56.2 (C_{quat}, C-4), 56.2 (+, OCH_3), 61.9 (–, OCH_2CH_3), 68.5 (+, C-13), 71.9 (C_{quat}, C-6), 80.8 (C_{quat}, C-12), 82.5 (C_{quat}, C-13), 122.4 (–, C-1), 126.6 (C_{quat}, C-2), 169.1 (C_{quat}, 2 *C*OOEt) ppm. MS (EI, 70 eV): *m*/*z* (%) = 347 (64) [M^+ – Br], 242 (20), 241 (58), 213 (26), 197 (21), 169 (67), 168 (38), 134 (38), 117 (56), 115 (36), 91 (85), 77 (46), 65 (47), 55 (53), 43 (86), 41 (100).

Diethyl 2-Bromo-14-ethyl-14-hydroxy-8-methoxy-1-hexadecene-6,12-diyne-4,4-dicarboxylate (10a): To a solution of **9** (1.08 g, 2.5 mmol) in THF (20 mL), kept at –78 °C, was added dropwise *n*-butyllithium (1.1 mL, 2.6 mmol, 2.4 M in hexane) and stirring was continued for 30 min. After adding diethyl ketone (259 mg, 3.0 mmol), the reaction mixture was warmed to ambient temperature. After stirring for an additional 2 h, the reaction mixture was added to water (50 mL), and the mixture was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (40 g of flash silica gel, column 2.5 × 20 cm, PE/Et_2O, 8:1) to afford 0.36 g (28%) of **10a** as a colorless oil, R_f (PE/Et_2O, 2:1) = 0.19. IR (film): $\tilde{\nu}$ = 3450 (OH), 2930, 2230 (C≡C), 1740 (C=O), 1625 (C=C), 1430, 1370, 1290, 1250, 1190, 1100, 1070, 960, 905, 870, 740 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.06 (t, ^3J = 7.0 Hz, 6 H, CH_2CH_3), 1.13 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.47–1.53 (m, 6 H, CH_2CH_3 and 10-H), 1.53–1.68 (m, 2 H, 9-H), 2.09 (t, ^3J = 6.7 Hz, 2 H, 11-H), 2.40 (s, 1 H, OH), 2.82 (d, ^5J = 1.7 Hz, 2 H, 5-H), 3.13 (s, 2 H, 3-H), 3.20 (s, 3 H, OCH_3), 3.80 (t, ^3J = 6.3 Hz, 1 H, 8-H), 4.08 (m, 4 H, OCH_2CH_3), 5.47 (d, ^2J = 1.5 Hz, 1 H, 1-H), 5.65 (br. s, 1 H, 1-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 8.3 (+, CH_2CH_3), 13.6 (+, OCH_2CH_3), 18.0 (–, C-11), 22.2 (–, C-5), 24.2 (–, C-10), 34.3 (–, C-9), 34.5 (–), 42.5 (–, C-3), 55.8 (+, OCH_3), 55.8 (C_{quat}, C-4), 61.6 (–, OCH_2CH_3), 70.4 (+, C-8), 71.6 (C_{quat}, C-6), 80.4 (C_{quat}, C-7), 82.3 (C_{quat}, C-13), 83.5 (C_{quat}, C-12), 122.0 (–, C-1), 126.3 (C_{quat}, C-2), 168.7 (C_{quat}, 2 *C*OOEt) ppm. MS (EI, 70 eV): *m*/*z* (%) = 485/483 (6/4) [M^+ – CH_2CH_3], 453/451 (4/3), 331 (4), 241 (6), 130 (10), 109 (4), 91 (14), 71 (11), 57 (100), 44 (23).

1-Methyl 10,10-Diethyl 12-Bromo-6-methoxy-12-tridecene-1,7-diyne-1,10,10-tricarboxylate (10b): A solution of lithiated **9** (4.7 mmol) was prepared as described for the preparation of **10a**. To this solution was added at –78 °C a solution of methyl chloroformate (3.76 mL, 46.8 mmol) in THF (70 mL), and stirring was continued at ambient temperature for 2 h. After work-up as for **10a**, the resulting residue was purified by column chromatography (55 g of flash silica gel, column 2.5 × 35 cm, PE/Et_2O, 8:1) to afford 1.36 g (60%) of **10b** as a colorless oil, R_f (PE/Et_2O, 2:1) = 0.25. IR (film): $\tilde{\nu}$ = 2900, 2250 (C≡C), 1730 (C=O), 1635 (C=C), 1440, 1375, 1025, 955, 915, 855, 765 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.19 (t, ^3J = 7.1 Hz, 6 H, CH_2CH_3), 1.64–1.68 (m, 4 H, 4- and 5-H), 2.29 (t, ^3J = 6.3 Hz, 2 H, 3-H), 2.89 (d, ^5J = 1.6 Hz, 2 H, 9-H), 3.20 (s, 2 H, 11-H), 3.26 (s, 3 H, OCH_3), 3.66 (s, 3 H, $COOCH_3$), 3.85 (br. s, 1 H, 6-H), 4.13 (m, 4 H, OCH_2CH_3), 5.53 (d, ^2J = 1.5 Hz, 1 H, 13-H), 5.70 (br. s, 1 H, 13-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.7 (+, CH_2CH_3), 18.2 (–, C-3), 22.3 (–, C-9), 23.2 (–, C-4), 34.5 (–, C-5), 42.7 (–, C-11), 52.2 (+, $COOCH_3$), 56.0 (+, OCH_3), 56.0 (C_{quat}, C-10), 61.7 (–, OCH_2CH_3), 70.4 (+, C-6), 73.1 (C_{quat}, C-8), 80.9 (C_{quat}, C-1), 82.1 (C_{quat}, C-7), 88.8 (C_{quat}, C-2), 122.1 (–, C-13), 126.4 (C_{quat}, C-12), 154 (C_{quat}, *C*OOMe), 168.8 (C_{quat}, 2 *C*OOEt) ppm. MS (EI, 70 eV): *m*/*z* (%) = 455 (2), 404 (17) [M^+ – Br], 299 (14), 295 (16), 286 (12), 280 (10), 271 (16), 169 (22), 167 (24), 165 (20), 161 (24), 147 (20), 137 (22), 115 (27), 111 (24), 105 (32), 91 (58), 85 (35), 79 (59), 71 (61), 59 (49), 45 (64), 43 (100).

3,9-Decadiyn-1-ol (12): *n*-Butyllithium (17.6 mL, 27.4 mmol, 1.56 M in hexane) at –78 °C was added dropwise to a solution of 1,7-octadiyne (3 g, 28.3 mmol) in THF (175 mL). After stirring for 30 min, boron trifluoride diethyl etherate ($BF_3{\cdot}Et_2O$) (3.5 mL, 27.8 mmol) was added to the resulting colorless suspension. The reaction mixture was stirred for an additional 15 min before adding ethylene oxide (14.11 mL, 283 mmol). After stirring the mixture for 2 h, the reaction was quenched at –78 °C by adding a saturated aqueous solution of ammonium chloride (120 mL), and the mixture was extracted with diethyl ether (4 × 100 mL). The combined ether fractions were dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography (60 g of silica gel, column 2.5 × 50 cm, and pentane/Et_2O, 2:1) to afford 2.5 g (60%) of **12** as a colorless liquid. R_f (pentane/Et_2O, 1:1) = 0.6. IR (film): $\tilde{\nu}$ = 3303,

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2950, 2863, 2116, 1431, 1330, 1272, 1186, 1038, 849, 621 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.60 (m, 4 H, 6,7-H), 1.80 (br. s, 1 H, OH), 1.94 (t, ^4J = 2.65 Hz, 1 H, 10-H), 2.15–2.23 (m, 4 H, 5,8-H), 2.41 (m, 2 H, 2-H), 3.66 (t, ^3J = 6.0 Hz, 2 H, 1-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 17.88 (–, C-5), 18.23 (–, C-8), 23.11 (–, C-2), 27.30 (–, C-6*), 27.48 (–, C-7*), 61.31 (–, C-1), 68.45 (–, C-10), 76.74 (C_{quat}, C-3), 81.97 (C_{quat}, C-4), 84.14 (C_{quat}, C-9) ppm. MS (DCI, NH_3): *m/z* (%) = 185 (93) [M + $N_2H_7^+$], 168 (100) [M + NH_4^+]. $C_{10}H_{14}O$ (150.1): calcd. C 79.96, H 9.39; found C 79.71, H 9.14.

3,9-Decadiynyl Methanesulfonate (13): Methanesulfonyl chloride (4.2 mL, 54 mmol) was added at –10 °C to a mixture of 3,9-decadiyn-1-ol (**12**)(5.4 g, 36 mmol), triethylamine (Et_3N) (10 mL, 72 mmol) and dichloromethane (120 mL). After stirring at –10 °C for 12 h, the reaction mixture was poured into water (120 mL), the two layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 30 mL). The combined organic phases were dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography (120 g of silica gel, column 2.5 × 80 cm, pentane/Et_2O, 2:1) to afford 7.0 g (85%) of **13** as a yellowish liquid. R_f (pentane/Et_2O, 1:1) = 0.6. IR (film): $\tilde{\nu}$ = 3289, 3026, 2940, 2856, 2115, 1734, 1356, 1175, 964, 904, 801, 649 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.54–1.67 (m, 4 H, 6,7-H), 1.94 (t, ^4J = 2.7 Hz, 1 H, 10-H), 2.13–2.23 (m, 4 H, 5,8-H), 2.6 (m, 2 H, 2-H), 3.03 (s, 3 H, CH_3SO_3), 4.25 (t, ^3J = 6.78 Hz, 2 H, 1-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 17.90 (–, C-2), 18.12 (–, C-5), 20.00 (–, C-8), 27.41 (–, C-6*), 27.58 (–, C-7*), 37.61 (+, CH_3SO_3), 67.85 (–, C-1), 68.51 (C_{quat}, C-10), 74.50 (C_{quat}, C-3), 82.43 (C_{quat}, C-4), 84.07 (C_{quat}, C-9) ppm. MS (DCI, NH_3): *m/z* (%) = 474 (64) [2 M + NH_4^+], 246.1 (100) [M + NH_4^+]. $C_{11}H_{16}O_3S$ (228.1): calcd. C 57.87, H 7.06; found C 57.97, H 6.91.

Dimethyl 2-(3′,9′-Decadiynyl)malonate (14): Dimethyl malonate (8.1 g, 61 mmol) was added dropwise at 50 °C to a suspension of sodium hydride (2.45 g, 61 mmol, 60% oil suspension) in DMF (200 mL). The resulting clear solution was transferred into a mixture of 3,9-decadiynyl methanesulfonate (**13**) (7.0 g, 30 mmol), potassium iodide (5.1 g, 30 mmol) and THF (200 mL). The resulting mixture was heated under reflux at 70 °C for 18 h. The reaction mixture was then treated with a saturated aqueous solution of ammonium chloride (200 mL), and the aqueous layer was extracted with diethyl ether (3 × 100 mL). The combined organic phases were dried ($MgSO_4$), concentrated, and the residue was purified by azeotropic Kugelrohr distillation (at 170 °C, 0.1 mm) after adding 3 drops of dimethoxymethane to produce 6.7 g (83%) of **14** as a colorless oil. An analytical sample was further purified by column chromatography (silica gel, 5:1 pentane/Et_2O). R_f (pentane/Et_2O, 5:1) = 0.16. IR (film): $\tilde{\nu}$ = 3304, 3004, 2955, 2865, 2843, 2116, 1762, 1728, 1433, 1360, 1250, 1150, 1050, 632 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.61 (m, 4 H, 6′,7′-H), 1.94 (t, ^4J = 2.7, 1 H, 10′-H), 2.08 (q, ^3J = 6.4, 2 H, 1′-H), 2.15–2.23 (m, 6 H, 2′,5′,8′-H), 3.61 (t, ^3J = 7.2 Hz, 1 H, 2-H), 3.74 (s, 3 H, $COOCH_3$) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 16.72 (–, C-2′), 17.94 (–, C-5′), 18.20 (–, C-8′), 27.44 (–, C-1′), 27.83 (–, C-6′*), 28.02 (–, C-7′*), 50.27 (+, C-2), 52.58 (+, $COOCH_3$), 68.39 (+, C-10′), 78.19 (C_{quat}, C-3′), 81.26 (C_{quat}, C-4′), 83.30 (C_{quat}, C-9′), 169.59 (C_{quat}, 2 $COOCH_3$) ppm. MS (DCI, NH_3): *m/z* (%) = 282 (100) [M + NH_4^+], 236 (2), 206 (4), 167 (8), 150 (8). $C_{15}H_{20}O_4$ (264.3): calcd. C 68.16, H 7.63; found C 68.15, H 7.43.

Dimethyl 2-(2′′-Bromoallyl)-2-(3′,9′-decadiynyl)malonate (15): Dimethyl 2-(3′,9′-decadiynyl)malonate (**14**) (6.4 g, 23.79 mmol) was added dropwise at 50 °C to a suspension of sodium hydride (0.95 g, 23.79 mmol, 60% oil suspension) in 1,2-dimethoxyethane(DME) (90 mL). To the resulting mixture were added 2,3-dibromopropene (7.13 g, 35.68 mmol) and DMF (10 mL). After heating under reflux at 70 °C for 20 h, the reaction mixture was cooled to ambient temperature, water (120 mL) was added, and the mixture extracted with diethyl ether (5 × 50 mL). The combined organic phases were dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography (200 g of silica gel, column 2.5 × 120 cm, pentane/dichloromethane, 5:4) to afford 7.8 g (85%) of **15** as a colorless oil. R_f (pentane/dichloromethane, 5:4) = 0.72. IR (film): $\tilde{\nu}$ = 3311, 2928, 2845, 2116, 1740, 1624, 1464, 1378, 1273, 1200, 1153, 898, 741 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.59 (m, 4 H, 6′, 7′-H), 1.94 (t, ^4J = 1.96 Hz, 1 H, 10′-H), 2.08–2.26 (m, 8 H, 1′,2′,5′,8′-H), 3.16 (s, 2 H, 1′′-H), 3.73 (s, 6 H, $COOCH_3$), 5.59 (d, ^2J = 1.78 Hz, 1 H, 3′′-H), 5.67 (d, ^2J = 1.67 Hz, 1 H, 3′′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.26 (–, C-2′), 17.94 (–, C-5′), 18.26 (–, C-8′), 27.48 (–, C-6′*), 27.79 (–, C-7′*), 31.15 (–, C-1′), 43.19 (–, C-1′′), 52.74 (+, $COOCH_3$), 56.45 (C_{quat}, C-2), 68.40 (C_{quat}, C-10′), 78.65 (C_{quat}, C-3′), 80.41 (C_{quat}, C-4′), 84.20 (C_{quat}, C-9′), 122.08 (–, C-3′′), 126.83 (C_{quat}, C-2′′), 170.54 (C_{quat}, 2 $COOCH_3$) ppm. MS (DCI, NH_3): *m/z* (%) = 784 (45) [2 M + NH_4^+], 400/402 (100/98) [M – H + NH_4^+], 383/385 (9/9) [M^+ + H], 303 (8) [M^+ – Br]. $C_{18}H_{23}BrO_4$ (383.2): calcd. C 56.41, H 6.05; found C 56.70, H 5.82.

Trimethyl 13-Bromo-13-tetradecene-1,7-diyne-1,11,11-tricarboxylate (16): A solution of LDA (14.8 mmol) in THF (25 mL) [prepared by dropwise addition, at –78 °C, of diisopropylamine (1.5 g, 14.8 mmol) to a solution of *n*-butyllithium (10 mL, 15.6 mmol, 1.56 M in hexane) in THF (25 mL) and stirring for 30 min] was added dropwise, at –78 °C, to a solution of dimethyl 2-(2′′-bromoallyl)-2-(3′,9′-decadiynyl)malonate (**15**) (5.4 g, 14.2 mmol) in THF (25 mL). After stirring for 30 min, HMPA (2.48 mL, 13.7 mmol) and methyl chloroformate (10.8 mL, 142 mmol) were added, stirring was continued at –78 °C for 1 h, and at room temperature for 2 h. The reaction was then quenched by addition of a saturated solution of ammonium chloride (50 mL), and the mixture was extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (100 g of silica gel, column 2.5 × 80 cm, employing a polarity gradient starting with 8:1 pentane/Et_2O until the starting materials were removed; then with 6:1 pentane/Et_2O and finally with 4:1 pentane/Et_2O to elute the product) to afford 2.8 g (44%) of **16** as a colorless oil. R_f (pentane/Et_2O, 4:1) = 0.36. IR (film): $\tilde{\nu}$ = 3002, 2953, 2865, 2236, 1736, 1708, 1625, 1433, 1274, 1179, 1152, 1080, 902, 753, 591 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.53–1.72 (m, 4 H, 4,5-H), 2.01–2.24 (m, 6 H, 6,9,10-H), 2.34 (t, ^3J = 6.80 Hz, 2 H, 3-H), 3.15 (s, 2 H, 12-H), 3.72 (s, 3 H, $COOCH_3$), 3.74 (s, 3 H, $COOCH_3$), 5.58 (d, ^2J = 1.78 Hz, 1 H, 14-H), 5.66 (d, ^2J = 1.62 Hz, 1 H, 14-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.24 (–, C-9), 18.20 (–, C-6), 18.21 (–, C-3), 26.50 (–, C-5), 27.75 (–, C-4), 31.12 (–, C-10), 43.19 (–, C-12), 52.57 (+, $COOCH_3$), 52.74 (+, $COOCH_3$), 56.43 (C_{quat}, C-11), 73.02 (C_{quat}, C-1), 78.93 (C_{quat}, C-8), 80.03 (C_{quat}, C-7), 89.30 (C_{quat}, C-2), 122.09 (–, C-14), 126.79 (C_{quat}, C-13), 154.18 (C_{quat}, $COOCH_3$), 170.52 (C_{quat}, 2 $COOCH_3$) ppm. MS (DCI, NH_3): *m/z* (%) = 460/458 (100/96) [M – H + NH_4^+], 340 (4), 208 (4). $C_{20}H_{25}BrO_6$ (441.3): calcd. C 54.43, H 5.71; found C 54.43, H 5.41.

2-[10′-(*tert*-Butyldimethylsilyl)deca-3′,9′-diynyloxy]tetrahydro-2*H*-pyran (19): To a solution of 2-(but-3-ynyloxy)tetrahydro-2*H*-pyran (**17**) (9.04 g, 58.6 mmol) in THF (120 mL) was added dropwise at –78 °C a solution of *n*-butyllithium (41.0 mL, 64.0 mmol, 1.5 M in hexane). After stirring at –78 °C for 30 min, 6-bromo-1-(*tert*-butyl-

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dimethylsilyl)hexyne (**18**) (17.62 g, 64.0 mmol) and HMPA (11.5 mL, 64.0 mmol) were added to the resulting solution. The reaction mixture was warmed to room temperature, and stirring was continued for 5 h. The mixture was then diluted with 50 mL of water, the two layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography (500 g of silica gel, column 8 × 60 cm, PE/Et_2O, 10:1) to afford 9.40 g (46%) of **19** as a colorless liquid. R_f (PE/Et_2O, 10:1) = 0.29. IR (film): $\tilde{\nu}$ = 2927, 2856, 2173, 1471, 1250, 1123, 1071, 1036, 839, 776, 681 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.06 [s, 6 H, $Si(CH_3)_2$], 0.91 [s, 9 H, $C(CH_3)_3$], 1.20–1.35 (m, 2 H, 6′-H), 1.50–1.70 (m, 6 H, 3,4,5-H), 2.16 (m, 2 H, 8′-H), 2.23 (m, 2 H, 5′-H), 2.44 (tt, ^3J = 7.2, ^5J = 2.4 Hz, 2 H, 2′-H), 3.52 (m, 2 H, 6-H), 3.80 (m, 2 H, 1′-H), 4.63 (m, 1 H, 2-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = –4.57 [$Si(CH_3)_2$], –4.49 [$Si(CH_3)_2$], 16.48 [$C(CH_3)_3$], 18.20 (C-2′), 19.35 (C-4*), 19.39 (C-8′*), 20.16 (C-5′), 25.41 (C-5), 26.00 [$C(CH_3)_3$], 27.65 (C-6′**), 27.89 (C-7′**), 30.53 (C-3), 62.11 (C-6), 66.14 (C-1′), 77.00 (C-3′), 80.69 (C-4′), 82.58 (C-10′), 98.55 (C-2), 107.67 (C-9′) ppm. $C_{21}H_{36}O_2Si$ (348.6).

10-Bromo-1-(*tert*-butyldimethylsilyl)deca-1,7-diyne (20): To a solution of triphenylphosphane (15.76 g, 60 mmol) in dichloromethane (150 mL) was added bromine (9.60 g, 60 mmol) dropwise at –20 °C. After stirring at –20 °C for 30 min, 2-[10′-(*tert*-butyldimethylsilyl)-deca-3′,9′-diynyloxy]tetrahydro-2*H*-pyran (**19**) (9.40 g, 27 mmol) was added to the colorless suspension of the triphenylphenylphosphane-bromine complex, and stirring was continued at room temperature for 20 h. The reaction mixture was then diluted with water (100 mL), the two layers were separated, and the aqueous layer was extracted with dichloromethane (100 mL). The organic layer was dried ($MgSO_4$), concentrated, and the resulting residue was purified by column chromatography (120 g of silica gel, column 5 × 35 cm, pentane) to afford 7.07 g (80%) of **20** as a colorless liquid. R_f (PE/Et_2O, 20:1) = 0.50. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.05 [s, 6 H, $Si(CH_3)_2$], 0.90 [s, 9 H, $C(CH_3)_3$], 1.55 (m, 4 H, 4,5-H), 2.1–2.3 (m, 4 H, 3,6-H), 2.68 (tt, ^3J = 7.4, ^5J = 2.4 Hz, 2 H, 9-H), 3.39 (t, ^3J = 7.4 Hz, 2 H, 10-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = –4.47 [2 $Si(CH_3)_2$], 16.50 [$C(CH_3)_3$], 18.15 [C-3,6], 23.30 (C-9), 26.05 [3 $C(CH_3)_3$], 27.63 (C-4*), 27.70 (C-5*), 30.32 (C-10), 77.21 (C-8), 82.06 (C-1), 82.71 (C-7), 107.51 (C-9) ppm. MS (DCI, NH_3): *m*/*z* (%) = 347/346/345/344 (20/100/21/95) [M + NH_4^+]. $C_{16}H_{27}BrSi$ (327.4).

Dimethyl 2-[10′-(*tert*-Butyldimethylsilyl)deca-3′,9′-diynyl]malonate (21): Dimethyl malonate (3.17 g, 24 mmol) was added dropwise at room temperature to a suspension of sodium hydride (0.63 g, 26 mmol, 60% oil suspension) in DMF (75 mL). The resulting clear solution was transferred into a solution of 10-bromo-1-(*tert*-butyldimethylsilyl)deca-1,7-diyne (**20**) (6.38 g, 19.5 mmol) in DMF (35 mL). After stirring for 36 h, the reaction mixture was treated with a saturated aqueous solution of ammonium chloride (100 mL), the two layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic phases were dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography (100 g of silica gel, column 2.5 × 50 cm, PE/Et_2O, 10:1) to afford 3.87 g (52%) of **21** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.19. IR (film): $\tilde{\nu}$ = 2951, 2855, 2172, 1737, 1635, 1250, 1155, 839, 776, 681 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.05 [s, 6 H, $Si(CH_3)_2$], 0.90 [s, 9 H, $C(CH_3)_3$], 1.55 (m, 4 H, 6′, 7′-H), 2.05 (dt, ^3J = 7.0, ^3J = 7.0 Hz, 2 H, 1′-H), 2.10–2.28 (m, 6 H, 2′,5′,8′-H), 3.58 (t, ^3J = 6.9 Hz, 1 H, 2-H), 3.72 (s, 6 H, OCH_3) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = –4.51 [2 $Si(CH_3)_2$], 16.45 [$C(CH_3)_3$], 16.68 (C-2′), 18.13 (C-5′), 19.30 (C-8′), 26.00 [3 $C(CH_3)_3$], 27.61 (C-1′*), 27.85 (C-6′*), 27.99 (C-7′*), 50.22 (C-2), 52.52 (2 OCH_3), 78.05 (C-3′*), 81.29 (C-4′*), 82.60 (C-10′*), 107.52 (C-9′*), 169.54 (2 C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 347 (5) [M^+ – OCH_3], 322 (23), 321 (100) [M^+ – C_4H_9], 261 (9), 173 (11), 89 (37), 73 (11), 59 (9). MS (DCI, NH_3): *m*/*z* (%) = 774 (62) [2 M + NH_4^+], 396 (100) [M + NH_4^+]. $C_{21}H_{34}O_4Si$ (378.6).

Dimethyl 2-Bromo-14-(*tert*-butyldimethylsilyl)tetradec-1-ene-7,13-diyne-4,4-dicarboxylate (22): Following the same procedure as for the preparation of **15**, to a suspension of sodium hydride (312 mg, 13 mmol, 60% oil suspension) in DME (24 mL) were added at 50 °C successively dimethyl 2-[10-(*tert*-butyldimethylsilyl)deca-3,9-diynyl]malonate (**21**) (4.45 g, 12.0 mmol) and 2,3-dibromopropene (2.60 g, 13 mmol). After work-up, the residue was purified by column chromatography (80 g of silica gel, column 2.5 × 40 cm, pentane/Et_2O, 20:1) to produce 4.56 g (52%) of **22** as a colorless oil. R_f (pentane/Et_2O, 10:1) = 0.25. IR (film): $\tilde{\nu}$ = 3951, 2857, 2172 (C≡C), 1738 (C=O), 1625, 1435, 1248, 1199, 838, 775, 680 cm^{-1}. ^1H NMR (250 MHz, C_6D_6): δ = 0.19 [s, 6 H, $Si(CH_3)_2$], 1.08 [s, 9 H, $C(CH_3)_3$], 1.45 (m, 4 H, 10, 11-H), 2.02 (m, 4 H, 5-H, CH_2), 2.23 (m, 2 H, CH_2), 2.52 (m, 2 H, CH_2), 3.27 (m, 2 H, 3-H), 3.33 (s, 6 H, OCH_3), 5.28 (m, 1 H, 1-H), 5.31 (d, ^2J = 1.70 Hz, 1 H, 1-H) ppm. ^{13}C NMR (62.9 MHz, C_6D_6): δ = –4.18 [2 $Si(CH_3)_2$], 14.79 (C-6), 16.75 [$C(CH_3)_3$], 18.51 (C-9), 19.57 (C-12), 26.33 [3 $C(CH_3)_3$], 27.79 (C-10*), 28.23 (C-11*), 31.86 (C-5), 43.60 (C-3), 52.24 (2 OCH_3), 56.76 (C-4), 79.09 (C-7**), 80.79 (C-8**), 82.84 (C-13), 108.11 (C-14), 122.06 (C-1), 127.43 (C-2), 170.40 (2 C=O) ppm. MS (DCI, NH_3): *m*/*z* = 517/516/515/514 (26/100/26/92) [M + NH_4^+]. $C_{24}H_{37}BrO_4Si$ (497.6): calcd. C 57.93, H 7.49; found C 57.50, H 7.41.

2-(3′,9′-Decadiynyl)-1,3-dioxolane (24): *n*-Butyllithium (12.5 mL, 18.7 mmol, 1.5 M in hexane) was added dropwise at –78 °C to a solution of 1,7-octadiyne (2.0 g, 18.8 mmol) in THF (40 mL). The mixture was stirred for 30 min and to the resulting colorless suspension was added sequentially HMPA (3.3 mL, 18.8 mmol) and 2-(1,3-dioxolan-2-yl)ethyl iodide (**23**) (4.5 g, 19.7 mmol). Stirring was continued at –78 °C for 2 h and at room temperature for 14 h. The reaction mixture was diluted with 150 mL of water, the two layers were separated, and the aqueous layer was extracted with diethyl ether (5 × 50 mL). The combined organic phases were dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography (70 g of silica gel, column 2.5 × 50 cm, pentane/Et_2O, 40:1) to afford 1.8 g (46%) of **24** as a colorless liquid. R_f (pentane/Et_2O, 40:1) $\tilde{\nu}$ = 0.16. IR (film): $\tilde{\nu}$ = 3287, 2944, 2863, 2712, 2657, 2116, 1434, 1412, 1330, 1147, 1127, 1072, 1045, 943, 898, 626 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.55–1.68 (m, 4 H, 6′,7′-H), 1.82 (dt, ^3J = 4.8, ^3J = 7.4, 2 H, 1′-H), 1.93 (t, ^4J = 2.6 Hz, 1 H, 10′-H), 3.81–3.91 (m, 4 H, O-CH_2CH_2-O), 4.95 (t, ^3J = 4.8 Hz, 1 H, 2-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.68 (–, C-2′), 17.92 (–, C-5′*), 18.20 (–, C-8′*), 27.46 (–, C-6′**), 27.88 (–, C-7′**), 33.30 (–, C-1′), 64.88 (–, O-CH_2CH_2-O), 68.34 (+, C-10′), 79.30 (C_{quat}, C-3′), 79.84 (C_{quat}, C-5′), 84.21 (C_{quat}, C-9′), 103.31 (+, C-2). MS (DCI, NH_3): *m*/*z* (%) = 430 (11) [2 M + NH_4^+], 224 (100) [M + NH_4^+], 207 (6) [M + H^+]. $C_{13}H_{18}O_2$ (206.1): calcd. C 75.69, H 8.75; found C 75.61, H 8.60.

2-Bromo-4-(*tert*-butyldimethylsilyloxy)tetradec-1-ene-7,13-diyne (26): To a suspension of tin powder (2 g, 17.2 mmol) in diethyl ether (16.6 mL) and water (6.5 mL) was added successively at room temperature, 2,3-dibromopropene (3.3 g, 16.6 mmol), 48% HBr (40 drops) and 2-(3,9-decadiynyl)-1,3-dioxolane (**24**) (2.5 g, 12.2 mmol). The mixture was vigorously stirred at room temperature for 5 d, then diluted with water (200 mL) and diethyl ether

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(200 mL), and the aqueous layer was extracted thoroughly with diethyl ether (12 × 100 mL). The combined ether fractions were dried ($MgSO_4$) and concentrated. The produced alcohol was immediately purified by column chromatography (70 g of silica gel, column 2.5 × 50 cm, employing a polarity gradient starting with 10:1 pentane/Et_2O to remove the starting material, then with 20:3 pentane/Et_2O) to afford 1.8 g (52%) of **25** as a colorless oil. R_f (pentane/Et_2O, 10:3) = 0.20. IR (film): $\tilde{\nu}$ = 3500, 3305, 2948, 2862, 2173, 2116, 1719, 1631, 1432, 1330, 1120, 1070, 893, 842, 634 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.59–1.69 (m, 4 H, 10,11-H), 1.94 (t, ^4J = 2.5 Hz, 1 H, 14-H), 2.07 (br. s, 1 H, OH), 2.15–2.24 (m, 4 H, 9, 12-H), 2.27–2.37 (m, 2 H, 6-H), 2.55 (d, ^3J = 6.30 Hz, 2 H, 3-H), 4.09 (m, 1 H, 4-H), 5.53 (d, ^2J = 1.5 Hz, 1 H, 1-H), 5.69 (d, ^2J = 0.87 Hz, 1 H, 1-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 15.33 (–, C-6), 17.94 (–, C-9), 18.21 (–, C-12), 27.49 (–, C-10*), 27.87 (–, C-11*), 35.11 (–, C-5), 49.12 (–, C-3), 68.31 (+, C-4), 68.41 (C_{quat}, C-14), 79.56 (C_{quat}, C-7), 80.67 (C_{quat}, C-8), 84.19 (C_{quat}, C-13), 119.60 (–, C-1), 130.44 (C_{quat}, C-2) ppm. MS (DCI, NH_3): *m/z* (%) = 584 (6) [2 M + NH_4^+], 301 (100) [M + NH_4^+].

tert-Butyldimethylsilyl chloride (1.2 g, 8 mmol) was added at 55 °C to a solution of freshly prepared 2-bromotetradec-1-ene-7,13-diyn-4-ol (**25**) (1.6 g, 5.67 mmol) and imidazole (1.3 g, 19.84 mmol) in DMF (20 mL). After stirring at 55 °C for 12 h, the reaction mixture was poured into water (100 mL) and the aqueous mixture was extracted with diethyl ether (3 × 50 mL). The combined ether layers were dried with $MgSO_4$, and concentrated. The residue was purified by column chromatography (50 g of silica gel, column 2.5 × 35 cm, pentane/Et_2O, 80:1) to afford 2 g (89%) of **26** as a colorless oil. R_f (pentane/Et_2O, 80:1) = 0.71. IR (film): $\tilde{\nu}$ = 3311, 2959, 2928, 2857, 1631, 1469, 1432, 1255, 1101, 1077, 1005, 836, 776, 628 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.087 [s, 6 H, $Si(CH_3)_2$], 0.91 [s, 9 H, $C(CH_3)_3$], 1.52–1.74 (m, 6 H, 5, 10, 11-H), 1.93 (t, ^4J = 2.6 Hz, 1 H, 14-H), 2.15–2.23 (m, 6 H, 6, 9, 12-H), 2.44–2.62 (m, 2 H, 3-H), 4.08 (m, 1 H, 4-H), 5.43 (d, ^2J = 1.47 Hz, 1 H, 1-H), 5.60 (br. s, 1 H, 1-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 4.62 [+, $Si(CH_3)_2$], - 4.40 [+, $Si(CH_3)_2$], 14.71 (–, C-6), 17.96 (–, C-9), 18.01 [C_{quat}, $C(CH_3)_3$], 18.22 (–, C-12), 25.74 [+, 3 $C(CH_3)_3$], 27.51 (–, C-10*), 27.95 (–, C-11*), 35.76 (–, C-5), 49.32 (–, C-3), 68.35 (C_{quat}, C-14), 68.82 (+, C-4), 79.93 (C_{quat}, C-7), 80.00 (C_{quat}, C-8), 84.21 (C_{quat}, C-13), 119.11 (–, C-1), 130.82 (C_{quat}, C-2) ppm. MS (DCI, NH_3): *m/z* (%) = 416 (100) [M + NH_4^+], 399 (2) [M + H^+], 336 (1) [M – Br + NH_4^+]. $C_{20}H_{33}BrOSi$ (397.2): calcd. C 60.44, H 8.37; found C 60.27, H 8.11.

Methyl 14-Bromo-12-(*tert*-butyldimethylsilyloxy)-14-pentadec-14-ene-2,8-diynoate (27): Following the same procedure as for the preparation of **16**, a solution of LDA (4.2 mmol) in THF (10 mL) [prepared by dropwise addition, at –78 °C, of diisopropylamine (0.42 g, 4.2 mmol) to a solution of *n*-butyllithium (2.8 mL, 4.2 mmol, 1.56 M in hexane) in THF (10 mL) and stirring for 30 min] was added dropwise, at –78 °C, to a solution of 2-bromo-4-(*tert*-butyldimethylsilyloxy)tetradec-1-ene-7,13-diyne (**26**) (1.5 g, 3.8 mmol) in THF (10 mL). After stirring for 30 min, HMPA (0.7 mL, 3.9 mmol) and methyl chloroformate (2.9 mL, 37 mmol) were added, stirring was continued at –78 °C for 1 h, then at room temperature for 2 h. After work-up as described for **16**, the resulting residue was purified by column chromatography (60 g of silica gel, column 2.5 × 35 cm, pentane/Et_2O, 40:1) to afford 0.7 g (40%) of **27** as a colorless oil. R_f (pentane/Et_2O, 20:1) = 0.33. IR (film): $\tilde{\nu}$ = 2950, 2928, 2843, 2173, 1750, 1250, 1073, 941, 823, 764 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.09 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $C(CH_3)_3$], 1.52–1.73 (m, 6 H, 5, 6,11-H), 2.15–2.23 (m, 4 H, 7, 10-H), 2.35 (t, ^3J = 6.8 Hz, 2 H, 4-H), 2.47–2.57 (m, 2 H, 13-H), 3.75 (s, 3 H, $COOCH_3$), 4.06 (m, 1 H, 12-H), 5.43 (d, ^2J = 1.5 Hz, 1 H, 15-H), 5.60 (d, ^2J = 1.13 Hz, 1 H, 15-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = –4.62 [+, $Si(CH_3)_2$], –4.40 [+, $Si(CH_3)_2$], 14.69 (–, C-10), 18.01 [C_{quat}, $C(CH_3)_3$], 18.15 (–, C-7), 18.23 (–, C-4), 25.82 [+, 3 $C(CH_3)_3$], 26.54 (–, C-6), 27.92 (–, C-5), 35.73 (–, C-11), 49.32 (–, C-13), 52.55 (+, $COOCH_3$), 68.82 (+, C-12), 77.19 (C_{quat}, C-2), 79.61 (C_{quat}, C-9), 80.24 (C_{quat}, C-8), 89.35 (C_{quat}, C-3), 119.16 (–, C-15), 130.79 (C_{quat}, C-14), 154 (C_{quat}, $COOCH_3$) ppm. MS (DCI, NH_3): *m/z* (%) = 472/474 (90/100) [M + NH_4^+], 457 (18) [M + H^+], 394 (18) [M – Br + NH_4^+].

10-(1′,3′-Dioxolan-2′-yl)-1-phenyl-1,7-decacdiyne (28): 2-(3′,9′-Decadiynyl)-1,3-dioxolane (**24**) (1.5 g, 7.28 mmol) was added to a mixture of dichlorobis(triphenylphosphane)palladium (30 mg, 0.042 mmol) [$PdCl_2(PPh_3)_2$], cuprous iodide (20 mg, 0.1 mmol) (CuI), triphenylphosphane (40 mg, 0.15 mmol), iodobenzene (1.5 g, 7.30 mmol) and triethylamine (50 mL)(Et_3N). The reaction mixture was stirred at 40 °C for 14 h, during which a substantial amount of a colorless solid was formed. The reaction was then quenched by addition of a saturated solution of ammonium chloride to the mixture, and the whole mixture was extracted with diethyl ether (5 × 50 mL). The combined ether layers were concentrated, and the residue was purified by column chromatography (70 g of silica gel, column 2.5 × 40 cm, pentane/Et_2O, 20:1) to afford 1.3 g (63%) of **28** as a colorless liquid. IR (film): $\tilde{\nu}$ = 3056, 2942, 2861, 2837, 2230, 1951, 1877, 1598, 1490, 1441, 1330, 1146, 1128, 1072, 1046, 943, 896, 758, 693, 525 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.61–1.73 (m, 4 H, 4,5-H), 1.84 (dt, ^3J = 4.8, ^3J = 7.4 Hz, 2 H, 10-H), 2.17–2.33 (m, 4 H, 3,6-H), 2.42 (t, ^3J = 6.7 Hz, 2 H, 9-H), 3.88–3.96 (m, 4 H, O-CH_2CH_2-O), 4.95 (t, ^3J = 4.7 Hz, 1 H, 2′-H), 7.24–7.41 (m, 5 H, phenyl-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.72 (–, C-9), 18.30 (–, C-6), 18.95 (–, C-3), 27.79 (–, C-5*), 28.11 (–, C-4*), 33.32 (–, C-10), 64.89 (–, O-CH_2CH_2-O), 79.29 (C_{quat}, C-8), 80.00 (C_{quat}, C-7**), 80.76 (C_{quat}, C-1**), 89.90 (C_{quat}, C-2), 103.33 (+, C-2′), 123.92 (C_{quat}, phenyl-C), 127.48 (+, *o*-phenyl-C), 128.14 (+, *m*-phenyl-C), 131.50 (+, *p*-phenyl-C) ppm. MS (DCI, NH_3): *m/z* (%) = 582 (2) [2 M + NH_4^+], 300 (100) [M + NH_4^+], 283 (6) [M + H^+]. $C_{19}H_{22}O_2$ (282.2): calcd. C 80.82, H 7.85; found C 80.56, H 7.62.

1-[13-Bromo-11-(*tert*-butyldimethylsilyloxy)tetradec-13-ene-1,7-diynyl]benzene (29): To a suspension of tin powder (0.73 g, 6.1 mmol) in a mixture of diethyl ether (8.7 mL) and water (3.5 mL) was added successively 2,3-dibromopropene (1.2 g, 6.1 mmol), 48% HBr (40 drops) and 10-(1′,3′-dioxolan-2′-yl)-1-phenyl-1,7-decadiyne (**28**) (1.1 g, 3.9 mmol). The mixture was vigorously stirred at room temperature for 5 d, then diluted with water (150 mL) and diethyl ether (150 mL), and the aqueous phase was extracted thoroughly with diethyl ether (10 × 100 mL). The combined ether layers were dried with $MgSO_4$, and concentrated. The produced alcohol was immediately purified by column chromatography [50 g of silica gel, column 2.5 × 40 cm, eluting with pentane/Et_2O (10:1) until the starting material had been removed and then raising the polarity to (20:3) to elute the product] to give 1.0 g (70%) of 2-bromo-14-phenyltetradec-1-ene-7,13-diyn-4-ol as a colorless oil. R_f (pentane/Et_2O, 20:3) = 0.18. IR (film): $\tilde{\nu}$ = 3500, 3079, 3056, 2948, 2901, 2838, 2228, 1949, 1876, 1631, 1490, 1439, 1331, 1121, 1068, 913, 891, 758, 693 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.62–1.72 (m, 6 H, 5, 10, 11-H), 2.08 (s, 1 H, OH), 2.22 (m, 2 H, 12-H), 2.33 (m, 2 H, 9-H), 2.43 (m, 2 H, 6-H), 2.55 (d, ^2J = 6.25 Hz, 2 H, 3-H), 4.10 (m, 1 H, 4-H), 5.53 (d, ^2J = 1.5 Hz, 1 H, 1-H), 5.69 (d, ^2J =

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0.85 Hz, 1 H, 1-H), 7.24–7.41 (m, 5 H, phenyl-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 15.37 (–, C-6), 18.30 (–, C-9), 18.97 (–, C-12), 27.81 (–, C-10*), 28.09 (–, C-11*), 35.09 (–, C-5), 49.11 (–, C-3), 68.38 (+, C-4), 79.55 (C_{quat}, C-7), 80.10 (C_{quat}, C-8**) 80.84 (C_{quat}, C-14**), 89.85 (C_{quat}, C-13), 119.64 (–, C-1), 123.90 (C_{quat}, phenyl-C), 127.50 (+, *o*-phenyl-C), 128.15 (+, *m*-phenyl-C), 130.42 (C_{quat}, C-2), 131.51 (+, *p*-phenyl-C) ppm. MS (DCI, NH_3): *m/z* (%) = 736 (1) [2 M + NH_4^+], 376/378 (100/98) [M + NH_4^+], 298 (11) [M – Br + NH_4^+].

Following the same procedure as applied for the preparation of **26**, *tert*-butyldimethylsilyl chloride (0.5 g, 3.33 mmol) was added at 55 °C to a solution of the freshly prepared 2-bromo-14-phenyltetradec-1-ene-7,13-diyn-4-ol (1 g, 2.77 mmol) and imidazole (0.65 g, 9.8 mmol) in DMF (10 mL). After stirring at 55 °C for 12 h, the reaction mixture was poured into water (70 mL), and the aqueous mixture was extracted with diethyl ether (3 × 40 mL). The combined ether layers were dried with $MgSO_4$ and concentrated. The residue was purified by column chromatography (50 g of silica gel, column 2.5 × 40 cm, pentane/Et_2O, 80:1) to afford 1.1 g (82%) of **29** as a colorless oil. R_f (pentane/Et_2O, 80:1) = 0.63. IR (film): $\tilde{\nu}$ = 3081, 3053, 2957, 2928, 2856, 2232, 1631, 1490, 1434, 1362, 1255, 1075, 1005, 890, 836, 777, 755, 692 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.095 [s, 6 H, $Si(CH_3)_2$], 0.88 [s, 9 H, $C(CH_3)_3$], 1.67–1.72 (m, 6 H, 4, 5,10-H), 2.22 (m, 4 H, 3,6-H), 2.40–2.47 (m, 2 H, 9-H), 2.51–2.57 (dd, ^2J = 6.4, ^2J = 4 Hz, 2 H, 12-H), 4.10 (m, 1 H, 11-H), 5.43 (d, ^2J = 1.3 Hz, 1 H, 14-H), 5.61 (d, ^2J = 1.3 Hz, 1 H, 14-H), 7.24–7.41 (m, 5 H, phenyl-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = –4.60 [+, $Si(CH_3)_2$], –4.40 [+, $Si(CH_3)_2$], 14.74 (–, C-9), 18.022 [C_{quat}, $C(CH_3)_3$], 18.32 (–, C-6), 18.99 (–, C-3), 25.84 [+, 3 $C(CH_3)_3$], 27.83 (–, C-5*), 28.18 (–, C-4*), 35.78 (–, C-10), 49.34 (–, C-12), 68.83 (–, C-10), 79.92 (C_{quat}, C-8), 80.13 (C_{quat}, C-7**), 80.78 (C_{quat}, C-1**), 89.88 (C_{quat}, C-2), 119.12 (–, C-14), 123.94 (C_{quat}, phenyl-C), 127.48 (+, *o*-phenyl-C), 128.14 (+, *m*-phenyl-C), 130.83 (C_{quat}, C-13), 131.51 (+, *p*-phenyl-C) ppm. MS (DCI, NH_3): *m/z* (%) = 490/492 (88/100) [M + NH_4^+], 412 (20) [M – Br + NH_4^+].

2′-Bromoallyl 3,9-Decadiynyl Ether (30): 3,9-Decadiyn-1-ol (**12**) (3.8 g, 25.25 mmol) was added dropwise at 70 °C to a suspension of sodium hydride (1.5 g, 38 mmol, 60% oil suspension) in THF (60 mL). 2,3-Dibromopropene (7.6 g, 38 mmol) was added, and the resulting mixture was heated at reflux at 70 °C for 12 h. After cooling to ambient temperatue, the reaction mixture was diluted with a saturated solution of ammonium chloride (80 mL) and extracted with diethyl ether (4 × 40 mL). The combined ether layers were dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (100 g of silica gel, column 2.5 × 60 cm, pentane/Et_2O, 20:1) to afford 2.9 g (42%) of **30** as a colorless oil. R_f (pentane/Et_2O, 10:1) = 0.40. IR (film): $\tilde{\nu}$ = 3304, 2948, 2907, 2864, 2116, 1735, 1640, 1434, 1333, 1110, 895, 638 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.57–1.65 [m, 4 H, 6 (7)-H], 1.94 (t, ^4J = 2.69 Hz, 1 H, 10-H), 2.15–2.23 (m, 4 H, 5,8-H), 2.43–2.49 (m, 2 H, 2-H), 3.56 (t, ^3J = 7.00 Hz, 2 H, 1-H), 4.12 (s, 2 H, 1′-H), 5.61 (dd, ^2J = 1.75, ^4J = 0.64 Hz, 1 H, 3′-H), 5.95 (d, ^2J = 1.36 Hz, 1 H, 3′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 17.93 (–, C-5*), 18.02 (–, C-8*), 20.10 (–, C-2), 27.47 (–, C-6**), 27.79 (–, C-7**), 68.36 (+, C-10), 69.07 (–, C-1), 74.83 (–, C-1′), 76.76 (C_{quat}, C-3), 80.97 (C_{quat}, C-4), 84.17 (C_{quat}, C-9), 117.34 (–, C-3′), 129.33 (C_{quat}, C-2′) ppm. MS (DCI, NH_3): *m/z* (%) = 286/288 (100/98) [M + NH_4^+]. $C_{13}H_{17}BrO$ (269.2): calcd. C 58.01, H 6.37; found C 58.32, H 6.25.

Methyl 11-(2′-Bromoallyloxy)-2,8-undecadiynoate (31): Following the same procedure as applied for the preparation of **16**, a solution of LDA (9.1 mmol) in THF (15 mL) [prepared by dropwise addition, at –78 °C, of diisopropylamine (0.92 g, 9.1 mmol) to a solution of *n*-butyllithium (4.5 mL, 9 mmol, 2 M in hexane) in THF (15 mL) and stirring for 30 min] was added dropwise at –78 °C to a solution of 2′-bromoallyl 3,9-decadiynyl ether (**30**) (2.3 g, 8.5 mmol) in THF (15 mL). After stirring for 30 min, HMPA (1.5 mL, 8.2 mmol) and methyl chloroformate (6.4 mL, 81.6 mmol) were added and stirring was continued at –78 °C for 1 h, then at room temperature for 2 h. After work-up as described for **16**, the resulting residue was purified by column chromatography (80 g of silica gel, column 2.5 × 40 cm, pentane/Et_2O, 10:1) to afford 1.9 g (68%) of **31** as a colorless oil. R_f (pentane/Et_2O, 20:1) = 0.12. IR (film): $\tilde{\nu}$ = 3409, 3305, 2954, 2866, 2235, 1719, 1639, 1434, 1251, 1109, 1078, 894, 752, 670 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.56–1.72 (m, 4 H, 5,6-H), 2.15–2.21 (m, 2 H, 7 H), 2.35 (t, ^3J = 6.83 Hz, 2 H, 4-H), 2.41–2.49 (m, 2 H, 10-H), 3.55 (t, ^3J = 6.91 Hz, 11-H), 3.75 (s, 3 H, $COOCH_3$), 4.12 (dd, ^2J = 2.26, ^4J = 1.05 Hz, 2 H, 1′-H), 5.61 (dd, ^2J = 1.75 Hz, ^4J = 0.95 Hz, 1 H, 3′-H), 5.94 (dd, ^2J = 2.69 Hz, ^4J = 1.28 Hz, 1 H, 3′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 18.16 (–, C-7*), 18.21 (–, C-4*), 20.09 (–, C-10), 26.52 (–, C-6), 27.76 (–, C-5), 52.52 (+, $COOCH_3$), 69.02 (–, C-11), 74.84 (–, C-1′), 77.08 (C_{quat}, C-2**), 77.17 (C_{quat}, C-9**), 80.58 (C_{quat}, C-8), 89.28 (C_{quat}, C-3), 117.37(–, C-3′), 129.33 (C_{quat}, C-2′), 159.94 (C_{quat}, $COOCH_3$) ppm. MS (DCI, NH_3): *m/z* (%) = 344/346 (98/100) [M – H + NH_4^+].

Diethyl 8-(1-Ethyl-1-hydroxypropyl)-13-methoxytricyclo[7.4.0. $0^{2,6}$]-trideca-1(9),2(6),7-triene-4,4-dicarboxylate (35b): According to GP method A, diethyl 2-bromo-14-ethyl-14-hydroxy-8-methoxyhexadec-1-ene-6,12-diyne-4,4-dicarboxylate (**10b**) (350 mg, 0.68 mmol) was added to a mixture of palladium acetate (9 mg, 0.04 mmol, 6 mol-%), triphenylphosphane (36 mg, 0.14 mmol, 20 mol-%) and potassium carbonate (189 mg, 1.36 mmol, 2 equiv.) in acetonitrile (10 mL). The mixture was heated at 120 °C for 2 h and the resulting residue after work-up was purified by column chromatography (8 g of flash silica gel, column 1 × 15 cm, PE/Et_2O, 2:1) to give 197 mg of **35b** (67%) as a light brown oil. R_f (PE/Et_2O, 2:1) = 0.42. IR (film): $\tilde{\nu}$ = 3550 (OH), 2940, 1720 (C=O), 1450, 1245, 1190, 1095, 910, 875 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.65 (m, ^3J = 7.0 Hz, 6 H, CH_2CH_3), 1.16 (m, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.51–2.11 (m, 8 H, 2 CH_2CH_3, 11, 12-H), 2.51–2.61 (m, 1 H, 10-H), 2.96–3.03 (m, 1 H, 10-H), 3.33 (s, 3 H, OCH_3), 3.43–3.58 (m, 4 H, 3,5-H), 4.05–4.17 (m, 4 H, OCH_2CH_3), 4.23 (br. s, 1 H, 13-H), 7.26 (br. s, 1 H, 7-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 7.9 (+, CH_2CH_3), 8.0 (+, CH_2CH_3), 13.7 (+, OCH_2CH_3), 18.4 (–, C-7), 25.9 (–, C-8*), 28.2 (–, C-6*), 33.1 (–, 2 CH_2CH_3), 39.2 (–, C-3), 40.4 (–, C-5), 55.5 (+, OCH_3), 60.0 (C_{quat}, C-4), 61.3 (–, OCH_2CH_3), 75.0 (+, C-13), 78.6 (C_{quat}, COH), 122.6 (+, C-7), 132.5 (C_{quat}, C-2), 134.2 (C_{quat}, C-9), 136.9 (C_{quat}, C-1), 139.1 (C_{quat}, C-6), 141.5 (C_{quat}, C-8), 171.4 (C_{quat}, C=O), 171.8 (C_{quat}, C=O) ppm. MS (EI, 70 eV): *m/z* (%) = 403 (39) [M^+ – CH_2CH_3], 400 (20), 371 (39), 309 (22), 108 (22), 86 (26), 79 (27), 57 (100). $C_{25}H_{36}O_6$ (432.2).

4,4-Diethyl 8-Methyl 13-Methoxytricyclo[7,4.0.$0^{2,6}$]trideca-1(9),2(6),7-triene-4,4,8-tricarboxylate (35a): According to GP method A, 10,10-diethyl 1-methyl 12-bromo-6-methoxytridec-12-ene-1,7-diyne-1,10,10-tricarboxylate (**10a**) (400 mg, 0.82 mmol) was added to a mixture of palladium acetate (6 mg, 0.026 mmol, 3 mol-%), triphenylphosphane (26 mg, 0.10 mmol, 12 mol-%) and potassium carbonate (229 mg, 1.64 mmol, 2 equiv.) in acetonitrile (10 mL). After heating the mixture at 120 °C for 14 h and work-up as described in GP method A, the resulting residue was purified by column chromatography (50 g of flash silica gel, column

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2.5 × 20 cm, PE/Et_2O, 4:1) to give 202 mg (61%) of **35a** as a colorless oil. R_f (PE/Et_2O, 1:1) = 0.35. IR (film): $\tilde{\nu}$ = 2940, 1730 (C=O), 1580 (C=C), 1440, 1375, 1080, 1020, 920, 870, 790 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.22 (m, 6 H, OCH_2CH_3), 1.50–1.85 (m, 3 H, 11, 12-H), 2.10–2.27 (m, 1 H, 12-H), 2.70–2.90 (m, 1 H, 10-H), 3.10–3.25 (dt, ^3J = 3.9, ^2J = 18.1 Hz, 1 H, 10-H), 3.42 (s, 3 H, OCH_3), 3.43–3.62 (m, 4 H, 3,5-H), 3.81 (s, 3 H, $COOCH_3$), 4.12–4.25 (m, 4 H, 2 OCH_2CH_3), 4.28 (t, ^3J = 3.6 Hz, 1 H, 13-H), 7.64 (s, 1 H, 7-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.9 (+, OCH_2CH_3), 17.6 (–, C-11), 25.5 (–, C-12), 27.9 (–, C-10), 39.4 (–, C-3), 40.0 (–, C-5), 51.5 (+, OCH_3), 55.8 (+, $COOCH_3$), 60.2 (C_{quat}, C-4), 61.6 (+, OCH_2CH_3), 74.3 (+, C-13), 125.6 (+, C-7), 129.0 (C_{quat}, C-8), 133.3 (C_{quat}, C-1), 137.5 (C_{quat}, C-9*), 138.2 (C_{quat}, C-6*), 145.3 (C_{quat}, C-2), 168.1 (C_{quat}, $COOCH_3$), 171.1 (C_{quat}, $COOCH_2CH_3$), 171.6 (C_{quat}, $COOCH_2CH_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 404 (0.2) [M^+], 388 (1), 373 (4) [$M^+ - OCH_3$], 299 (28), 167 (13), 165 (12), 140 (26), 112 (11), 110 (14), 91 (20), 45 (24), 44 (100). HRMS: calcd. for $C_{22}H_{28}O_7$ 404.183506 (correct mass).

Dimethyl 9-[*tert*-Butyl(dimethyl)silyl]tricyclo[8.4.0.0^{2,7}]tetradeca-1,7,9-triene-5,5-dicarboxylate (36): According to GP method A, dimethyl 2-bromo-14-(*tert*-butyldimethylsilyl)-1-tetradecen-7,13-diyne-4,4-dicarboxylate (**22**) (249 mg, 0.50 mmol) was added to a mixture of palladium acetate (11 mg, 0.05 mmol, 10 mol-%), triphenylphosphane (33 mg, 0.13 mmol, 25 mol-%) and potassium carbonate (207 mg, 1.5 mmol, 3 equiv.) in acetonitrile (5 mL). After heating the reaction mixture at 60 °C for 20 h and work-up as described in the GP, the resulting residue was purified by column chromatography (20 g of flash silica gel, column 2 × 35 cm, hexane/Et_2O, 10:1) to give 163 mg (79%) of **36** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.15. IR (film): $\tilde{\nu}$ = 2978, 2868, 1741 (C=O), 1638, 1444, 1383, 1351, 1277, 1044, 935, 846 cm^{-1}. ^{1}HNMR (250 MHz, $CDCl_3$): δ = 0.50 [m, 6 H, $Si(CH_3)_2$], 1.07 [s, 9 H, $C(CH_3)_3$], 1.95 (m, 4 H, 12, 13-H), 2.53 (t, ^3J = 6.6 Hz, 2 H, 4-H), 2.74 (t, ^3J = 6.0 Hz, 2 H, 11-H), 2.83 (t, ^3J = 6.6 Hz, 2 H, 3-H), 3.00 (t, ^3J = 6.0 Hz, 2 H, 14-H), 3.47 (s, 2 H, 6-H), 3.91 (s, 6 H, OCH_3), 7.08 (s, 1 H, 8-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = –2.61 [+, 2 $Si(CH_3)_2$], 17.97 [C_{quat}, $C(CH_3)_3$], 22.85 (–, C-12*), 23.00 (–, C-13*), 23.37 (–, C-3), 26.73 (–, C-11), 27.00 [+, 3 $C(CH_3)_3$], 28.21 (–, C-4), 32.08 (–, C-14), 35.14 (–, C-6), 52.64 (+, 2 OCH_3), 53.10 (C_{quat}, C-5), 129.07 (C_{quat}), 133.62 (C_{quat}), 133.94 (C_{quat}), 134.31 (C_{quat}), 134.47 (+, C-8), 141.13 (C_{quat}), 171.81 (C_{quat}, 2 C=O) ppm. MS (DCI, NH_3): *m*/*z* (%) = 850 (17) [2 M + NH_4^+], 434 (100) [M + NH_4^+]. $C_{24}H_{36}O_4Si$ (416.6): calcd. C 69.16, H 8.71; found C 69.51, H 8.97.

5-(*tert*-Butyldimethylsilyloxy)-9-phenyltricyclo[8.4.0.0^{2,7}]tetradeca-1,7,9-triene (37): Following GP method B, palladium acetate (9.48 mg, 0.042 mmol) was added at 80 °C to a degassed mixture of triphenylphosphane (28 mg, 0.10 mmol), sodium formate (34.4 mg, 0.50 mmol), 1-[13′-bromo-11′-(*tert*-butyldimethylsilyloxy)-13′-tetradecene-1′,7′-diynyl]benzene (**29**) (200 mg, 0.42 mmol) and DMF (5 mL). After stirring at 80 °C for 5 h, the reaction mixture was poured into water (30 mL), and the aqueous mixture was extracted with diethyl ether (3 × 20 mL). The combined ether layers were dried ($MgSO_4$), concentrated, and the residue was purified by thick-layer chromatography using 20 × 20 cm plates coated with silica gel, type 60 PF_{254} containing $CaSO_4$, eluting with pentane/dichloromethane, 2:1. The third fraction from the top of the plates afforded 25 mg (15%) of **37** as a yellow oil. R_f (pentane/dichloromethane, 2:1) = 0.55. IR (film): $\tilde{\nu}$ = 3057, 2927, 2856, 1462, 1251, 1095, 882, 773 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.12 [s, 6 H, $Si(CH_3)_2$], 0.94 [s, 9 H, $C(CH_3)_3$], 1.60–1.72 (m, 2 H, 3-H), 1.76–1.92 (m, 3 H, 11,14-H), 2.10 (m, 1 H, 14-H), 2.56 (t, ^3J = 10 Hz, 2 H, 4-H), 2.58–2.74 (m, 2 H, 13-H), 2.74–2.88 (m, 3 H, 6,12-H), 2.96 (dd, ^2J = 4, ^3J = 15 Hz, 1 H, 6-H), 4.08 (m, 1 H, 5-H), 6.84 (s, 1 H, 8-H), 7.25–7.40 (m, 5 H, Ph-H) ppm. ^{13}C NMR (150.82 MHz, $CDCl_3$, APT): δ = –4.62 [+, $Si(CH_3)_2$], –4.59 [+, $Si(CH_3)_2$], 18.30 [–, $C(CH_3)_3$], 22.90 (–, C-3), 23.15 (–, C-11), 25.87 (–, C-12), 25.95 [+, 3 $C(CH_3)_3$], 27.02 (–, C-13), 28.83 (–, C-4), 32.60 (–, C-14), 39.55 (–, C-6), 68.13 (+, C-5), 126.53 (+, Ph-C), 127.91 (+, Ph-C), 128.12 (+, Ph-C), 128.44 (+, Ph-C), 128.49 (+, Ph-C), 128.52 (+, Ph-C), 128.73 (+, Ph-C), 129.27 (+, C-8), 132.22 (–, C-1), 132.37 (–, C-2), 133.53 (–, C-7), 133.66 (+, Ph-C), 133.78 (+, Ph-C), 135.22 (–, C-10), 139.95 (–, Ph-C), 142.06 (–, C-9) ppm. MS (DCI, NH_3): *m*/*z* (%) = 410 (100) [M + NH_4^+], 495 (26) [(M – CH_3) + NH_4^+], 352 (7) [M + H – $C(CH_3)_3$ + NH_4^+], 296 (12) [(M – *t*$BuMe_2Si$) + NH_4^+], 279 (16) [M – H – *t*$BuMe_2SiO$ + NH_4^+], 263 (27). $C_{26}H_{36}OSi$ (392.6): calcd. C 79.53, H 9.24; found C 79.41, H 9.08.

Trimethyl Tetracyclo[8.4.0.0^{1,3}.0^{4,9}]tetradeca-4,9-diene-3,6,6-tricarboxylate (38): Following GP method A, palladium acetate (150 mg, 0.66 mmol) was added at 60 °C to a degassed mixture of triphenylphosphane (430 mg, 1.64 mmol), of potassium carbonate (2.72 g, 19.7 mmol), trimethyl 13-bromo-13-tetradecene-1,7-diyne-1,11,11-tricarboxylate (**16**) (2.9 g, 6.59 mmol) and acetonitrile (100 mL). After stirring the reaction mixture at 60 °C for 20 h and work-up as described in the GP, the residue was purified by column chromatography (60 g of silica gel, column 2 × 30 cm, pentane/Et_2O, 4:1) to afford 1.3 g (54%) of **38** as an orange oil. R_f (pentane/Et_2O, 4:1) = 0.17. IR (film): $\tilde{\nu}$ = 2996, 2954, 2855, 1755, 1715, 1433, 1302, 1226, 1197, 1154, 1076, 1062, 851, 833, 735, 702 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.07 (d, ^2J = 2.9 Hz, 1 H, 2-H), 1.24 (m, 1 H, 12-H), 1.46–1.56 (m, 1 H, 12-H), 1.68 (dt, ^2J = 2.8, ^3J = 15 Hz, 1 H, 14-H), 1.8–1.89 (m, 2 H, 11, 14-H), 1.95 (d, ^2J = 3.0 Hz, 1 H, 2-H), 2.00–2.37 (m, 4 H, 7,8,13-H), 2.40–2.61 (m, 3 H, 8, 11, 13-H), 3.70 (s, 3 H, $COOCH_3$), 3.72 (s, 3 H, $COOCH_3$), 3.75 (s, 3 H, $COOCH_3$), 6.09 (s, 1 H, 5-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.15 (–, C-8), 24.82 (–, C-12), 24.93 (–, C-11), 25.36 (–, C-13), 27.98 (–, C-14), 28.70 (–, C-7), 36.65 (C_{quat}, C-3), 39.29 (–, C-2), 45.88 (C_{quat}, C-1), 51.80 (+, $COOCH_3$), 52.68 (+, $COOCH_3$), 52.82 (+, $COOCH_3$), 55.28 (C_{quat}, C-6), 115.88 (+, C-5), 126.03 (C_{quat}, C-9), 143.53 (C_{quat}, C-4), 144.75 (C_{quat}, C-10), 170.96 (C_{quat}, $COOCH_3$), 171.35 (C_{quat}, $COOCH_3$), 171.72 (C_{quat}, $COOCH_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 360 (10) [M^+], 328 (24) [$M^+ - CH_3OH$], 301 (30) [$M^+ - COOCH_3$], 269 (46) [$M^+ - CH_3OH - COOCH_3$], 241 (39), 209 (20), 159 (30), 115 (72), 74 (79), 59 (100), 45 (64), 43 (27). $C_{20}H_{24}O_6$(360.4): calcd. C 66.65, H 6.43; found C 66.76, H 6.43.

Methyl 13-(*tert*-Butyldimethylsilyloxy)tetracyclo[8.4.0.0^{1,3}.0^{4,9}]-tetradeca-4,9-diene-3-carboxylate (39): Following GP method A, palladium acetate (9.8 mg, 0.050 mmol) was added at 60 °C to a degassed mixture of triphenylphosphane (29 mg, 0.11 mmol), potassium carbonate (182.6 mg, 1.3 mmol), methyl-14-bromo-12-(*tert*-butyldimethylsilyloxy)-14-pentadecene-2,8-diynoate (**27**) (200 mg, 0.44 mmol) and acetonitrile (5 mL). After heating the mixture at 60 °C for 18 h and work-up as described in the GP, the residue was purified by thick-layer chromatography using 20 × 20 cm plates coated with silica gel, type 60 PF_{254} containing $CaSO_4$. The plates were developed twice, first eluting with pentane/dichloromethane, 2:1, then with pentane/Et_2O, 10:1. The first fraction from the top of the plates afforded 32 mg (19%) of 2:1 of a mixture of diastereomers of **39** as a colorless oil. R_f (pentane/Et_2O, 5:1) = 0.12. IR (film): $\tilde{\nu}$ = 2957, 2854, 2240, 1734, 1437, 1255, 1202, 835, 777, 736 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.04 [s, 6 H,

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$Si(CH_3)_2$], 0.88 [s, 9 H, $C(CH_3)_3$], 1.03 (d, ^2J = 3.1 Hz, 1 H, 2-H), 1.40 (m, 1 H, 14-H), 1.54–1.72 (m, 1 H, 7-H), 1.74 (t, ^3J = 4 Hz, 1 H, 8-H), 1.80 (m, 3 H, 10, 14-H), 1.90 (d, ^2J = 3.15 Hz, 1 H, 2-H), 2.00 (m, 1 H, 8-H), 2.10 (m, 1 H, 6-H), 2.20–2.34 (m, 3 H, 6, 7, 11-H), 2.50 (d, ^3J = 5 Hz, 1 H, 11-H), 3.70 (s, 3 H, $COOCH_3$), 4.24 (br. s, 1 H, 13-H), 5.88 (t, ^3J = 5.5 Hz, 1 H, 5-H) ppm. ^{13}C NMR (125.705 MHz, $CDCl_3$, APT): δ = –4.88 [+, 2 $Si(CH_3)_2$], 17.99 [–, $C(CH_3)_3$], 19.10 (–, C-11), 22.46 (–, C-7), 22.65 (–, C-8), 25.43 (–, C-6), 25.75 [+, 3 $C(CH_3)_3$], 31.68 (–, C-14), 34.82 (–, C-12), 35.53 (–, C-3), 38.77 (–, C-2), 43.37 (–, C-1), 51.63 (+, $COOCH_3$), 66.77 (+, C-13), 120.52 (+, C-5), 128.21 (–, C-9), 139.45 (–, C-10), 142.12 (–, C-4), 171.92 (–, $COOCH_3$) ppm. MS (DCI, NH_3): *m*/*z* (%) = 392 (100) [M + NH_4^+], 375 (70) [M + H^+], 260 (8) [M^+ – *t*Bu-Me_2Si]. $C_{22}H_{34}O_3Si$ (374.6): calcd. C 70.54, H 9.15; found C 70.42, H 9.03.

Methyl 1,4,7,8,9,10-Hexahydro-2*H*-benzo[*f*]isochromene-6-carboxylate (41) and Methyl 1,5,5a,7,8,9-Hexahydro-2*H*-cyclopropa[2,3]indeno[2,1-*c*]pyran-5a-carboxylate (40): Following GP method A, palladium acetate (34 mg, 0.15 mmol) was added to a mixture of triphenylphosphane (99.8 mg, 0.38 mmol), potassium carbonate (630 mg, 4.5 mmol), methyl 11-(2′-bromoallyloxy)-2,8-undecadiynoate (**31**) (500 mg, 1.5 mmol) and acetonitrile (30 mL). After stirring the reaction mixture at 106 °C for 18 h and work-up as described in the GP, the residue was purified by thick-layer chromatography using 20 × 20 cm plates coated with silica gel type 60 PF_{254} containing $CaSO_4$. The plates were eluted twice with pentane/dichloromethane, 5:1, and once with pentane/Et_2O, (10:1) to afford two fractions:

I: 35 mg (10%) of **41** as a colorless viscous oil. R_f (pentane/Et_2O, 5:1) = 0.23. IR (film): $\tilde{\nu}$ = 2938, 1719, 1430, 1292, 1202, 1184, 1155, 1017, 925, 778 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.68–1.77 (m, 2 H, 8-H), 1.78–1.84 (m, 2 H, 9-H), 2.57 (t, ^3J = 5.5 Hz, 2 H, 10-H), 2.64 (t, ^3J = 5.6 Hz, 2 H, 1-H), 3.01 (t, ^3J = 6 Hz, 2 H, 7-H), 3.82 (s, 3 H, $COOCH_3$), 4.00 (t, ^3J = 6.1 Hz, 2 H, 2-H), 4.71 (s, 2 H, 4-H), 7.34 (s, 1 H, 5-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 22.37 (–, C-9), 22.61 (–, C-8), 26.08 (–, C-1), 26.55 (–, C-10), 28.19 (–, C-7), 51.77 (+, $COOCH_3$), 65.21 (–, C-2), 67.97 (–, C-4), 123.86 (+, C-5), 127.77 (C_{quat}), 131.59 (C_{quat}), 136.00 (C_{quat}), 136.50 (C_{quat}), 136.60 (C_{quat}), 168.42 (C_{quat}, $COOCH_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 246 (100) [M^+], 231 (21) [M^+ – CH_3], 214 (88) [M^+ – OCH_3], 187 (77) [M^+ – $COOCH_3$], 159 (36), 157 (19) [M^+ – $COOCH_3$ – H_2C=O], 141 (17), 129 (25), 115 (23), 91 (16). HRMS: Calcd. for $C_{15}H_{18}O_3$ (246.1): 246.1256 (correct mass).

II: 80 mg (21%) of **40** as a colorless oil. R_f (pentane/Et_2O, 5:1) = 0.18. IR (film): $\tilde{\nu}$ = 2992, 2926, 2857, 2827, 1715, 1436, 1382, 1363, 1298, 1247, 1221, 1199, 1163, 1082, 1050, 971, 855, 731, 666, 611 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.08 (d, ^2J = 3.1 Hz, 1 H, 5-H), 1.63 (m, 2 H, 8-H), 2.02 (d, ^2J = 3 Hz, 5-H), 2.05–2.15 (m, 2 H, 7,9-H), 2.23 (m, 1 H, 7-H), 2.30 (m, 1 H, 9-H), 2.37 (dt, $^3J_{ax\text{-}ax}$ = ^2J = 10, ^3Jax-eq = 5 Hz, 1 H, 2-H), 3.67 (s, 3 H, $COOCH_3$), 3.74 (d, ^2J = 12 Hz, 1 H, 4-H), 3.99 (d, ^2J = 12 Hz, 1 H, 4-H), 4.10 (ddd, ^2J = 11, $^3J_{eq\text{-}eq}$ = 5.5, ^3Jeq-ax = 2 Hz, 1 H, 2-H), 6.0 (t, ^3J = 4 Hz, 1 H, 6-H) ppm. ^{13}C NMR (150.82 MHz, $CDCl_3$, DEPT): δ = 22.19 (–, C-8), 22.52 (–, C-9), 25.34 (–, C-7), 26.23 (–, C-1), 35.52 (C_{quat}, C-5a), 37.30 (–, C-5), 42.87 (C_{quat}, C-4a), 51.71 (+, $COOCH_3$), 66.86 (–, C-2), 70.03 (–, C-4), 121.78 (+, C-6), 130.30 (C_{quat}, C-9a), 134.77 (C_{quat}, C-9b), 141.08 (C_{quat}, C-5b), 171.30 (C_{quat}, $COOCH_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 246 (23) [M^+], 215 (6) [M^+ – OCH_3], 187 (100) [M^+ – $COOCH_3$], 157 (43) [M^+ – $COOCH_3$ – H_2C=O], 141 (14), 129 (25), 115 (12). HRMS: Calcd. for $C_{15}H_{18}O_3$ (246.1): 246.1256 (correct mass).

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[1] For comprehensive reviews see: a) *Metal-Catalyzed Cross-Coupling Reactions, 2nd Completely Revised Edition* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**; b) *Handbook of Palladium Chemistry for Organic Synthesis* (Eds: E. Negishi, A. de Meijere) Wiley, New York, **2002**.

[2] For examples of such metal-catalyzed processes see: a) Ruthenium-catalyzed non-metathesis reactions: B. M. Trost, F. D. Toste, A. B. Pinkerton, *Chem. Rev.* **2001**, *101*, 2067–2096; b) Ruthenium-catalyzed metathesis reactions: T. M. Trenka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18–29; c) Nickel-catalyzed reactions: S. Ikeda, *Acc. Chem. Res.* **2000**, *33*, 511–519; d) Cobalt-catalyzed reactions: K. C. Nicolaou, E. J. Sorensen in *Classics in Total Synthesis*, Wiley-VCH, Weinheim, **1996**, pp. 153–166; e) F. Slowinski, C. Aubert, M. Malacria, *Eur. J. Org. Chem.* **2001**, 3491–3500, and references cited therein.

[3] a) L. F. Tietze, U. Beifuss, *Angew. Chem.* **1993**, *105*, 137–170; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 131–163; b) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115–136; c) L. F. Tietze, G. Brasche, K. M. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**.

[4] a) F. E. Meyer, P. J. Parsons, A. de Meijere, *J. Org. Chem.* **1991**, *56*, 6487–6488; b) F. E. Meyer, H. Henniges, A. de Meijere, *Tetrahedron Lett.* **1992**, *33*, 8039–8042; c) F. E. Meyer, J. Brandenburg, P. J. Parsons, A. de Meijere, *J. Chem. Soc., Chem. Commun.* **1992**, 390–392; d) F. E. Meyer, K. H. Ang, A. G. Steinig, A. de Meijere, *Synlett* **1994**, 191–193; e) K. H. Ang, S. Bräse, A. G. Steinig, F. E. Meyer, A. Llebaria, K. Voigt, A. de Meijere, *Tetrahedron* **1996**, *52*, 11503–11528; f) S. Schweizer, Z.-Z. Song, F. E. Meyer, P. J. Parsons, A. de Meijere, *Angew. Chem.* **1999**, *111*, 1550–1552; *Angew. Chem. Int. Ed.* **1999**, *38*, 1452–1454; for reviews see: g) A. de Meijere, P. von Zezschwitz, S. Bräse, *Acc. Chem. Res.* **2005**, *38*, 413–422; h) A. de Meijere, P. von Zezschwitz, H. Nüske, B. Stulgies, *J. Organomet. Chem.* **2002**, *653*, 129–140; P. von Zezschwitz, A. de Meijere, *Domino-Heck Pericyclic Reactions* in *Top. Organomet. Chem*. Springer, Berlin **2006**, pp. 49–89.

[5] a) Y. Zhang, E. Negishi, *J. Am. Chem. Soc.* **1989**, *111*, 3454–3456; b) Y. Zhang, G. Wu, G. Agnel, E. Negishi, *J. Am. Chem. Soc.* **1990**, *112*, 8590–8592.

[6] a) A. de Meijere, F. E. Meyer, *Angew. Chem.* **1994**, *106*, 2473–2506; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2379–2411; b) S. Bräse, A. de Meijere, in *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: A. de Meijere; F. Diederich), Wiley-VCH, Weinheim, **2004**, pp. 217–315; c) J. T. Link, L. Overman, in *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**, pp. 231–269.

[7] a) B. M. Trost, *Acc. Chem. Res.* **1990**, *23*, 34–42; b) B. M. Trost, M. J. Krische, *Synlett* **1998**, 1–16; c) B. M. Trost, Y. Li, *J. Am. Chem. Soc.* **1996**, *118*, 6625–6633; d) B. M. Trost, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259–281; e) B. M. Trost, D. L. Romero, F. Rise, *J. Am. Chem. Soc.* **1994**, *116*, 4268–4278; f) B. M. Trost, M. Lautens, C. Chan, D. T. MacPherson, *J. Am. Chem. Soc.* **1994**, *116*, 4255–4267; g) L. J. van Boxtel, S. Körbe, M. Noltemeyer, A. de Meijere, *Eur. J. Org. Chem.* **2001**, 2283–2292.

[8] For preliminary results of a fraction of this report see: a) F. E. Meyer, A. de Meijere, *Synlett* **1991**, 777–778; b) S. Schweizer, M. Schelper, C. Thies, P. J. Parsons, M. Noltemeyer, A. de Meijere, *Synlett* **2001**, 920–922.

[9] H. Henniges, F. E. Meyer, U. Schick, F. Funke, P. J. Parsons, A. de Meijere, *Tetrahedron* **1996**, *52*, 11545–11578.

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[10] H. Stetter, E. Reske, *Chem. Ber.* **1970**, *103*, 634–644.
[11] F. D. Gunstone, P. J. Sykes, *J. Chem. Soc.* **1962**, 3055–3058.
[12] S. Girard, P. Deslongchamps, *Can. J. Chem.* **1992**, *70*, 1256–1273.
[13] P. E. Sonnet, *Synth. Commun.* **1976**, *6*, 21–26.
[14] G. L. Larson, R. J. Klesse, *J. Org. Chem.* **1985**, *50*, 3627.
[15] T. Mandai, J. Nokami, T. Yano, Y. Yoshinaga, J. Otera, *J. Org. Chem.* **1984**, *49*, 172–174.
[16] E. Negishi, L. S. Harring, Z. Owczarczyk, M. M. Mohamud, M. Mehmet, *Tetrahedron Lett.* **1992**, *33*, 3253–3256.
[17] B. M. Trost, Y. Shi, *J. Am. Chem. Soc.* **1993**, *115*, 12491–12509.
[18] Review, see: A. Kirby, *Adv. Phys. Org. Chem.* **1980**, *17*, 183–279.

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