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Palladium-Catalyzed Oligocyclizations of 2-Bromoalka-1,(*n*+*m*+1)-dien-(*n*+1)-ynes – Influence of Tether Lengths and Substituents on the Outcome of the Reaction (Part II)

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Dedicated to Professor Dr. Carmen Najera on the occasion of her 60th birthday

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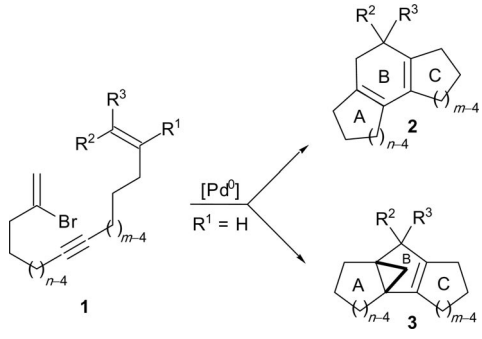
The cascade reaction modes and hence the outcomes of the palladium-catalyzed oligocyclizations of various 2-bromoalka-1,(*n*+*m*+1)-diene-(*n*+1)-yne substrates were found to be highly dependent on the tether lengths between the multiple bond fragments, and on the nature of the substituent at the non-brominated vinylic terminus. Just like 2-bromododeca-1,11-dien-6-ynes with their two three-atom tethers, 2-bromotrideca-1,12-dien-7-ynes **8** and 2-bromotetradeca-1,13-dien-8-ynes **17**, with combinations of four- and three- as well as five- and three-atom tethers, under Heck-type reaction conditions undergo, after the initial oxidative addition step, two consecutive *n-exo-dig* and *m-exo-trig* carbopalladations followed by β-hydride elimination and ensuing 6π-electrocyclization to furnish tricyclic bisannelated cyclohexadiene derivatives, such as **37** and **40**, in moderate yields (30 and 29%). On the other hand, when 2-bromoalka-1,(*n*+*m*+1)-dienynes with a four-, five- or even a six-atom tether between the bromoene and the yne moiety, and a four-atom tether between the yne and the terminal ene unit, such as **34**, **35** and **36**, are subjected to Heck-type reaction conditions, they undergo a cascade oligocyclization involving a 5-*exo-trig*- and ensuing 3-*exo-trig*-carbopalladation as the fourth and fifth steps before the terminating β-hydride elimination, eventually leading to tetracyclic skeletons such as **43**, **44** and **45** with a bridging three-membered ring in yields of 74, 76 and 32%, respectively.

Introduction

Transition metal-catalyzed so-called cascade or domino reactions[1] are efficient ways of constructing complex carbon frameworks in a single one-pot operation. In this context, several transition metals[2] have been utilized to induce different cascade modes to provide a diversity of complex, mostly oligocyclic compounds the access to which, otherwise, would be difficult. Yet, palladium-catalyzed cascade oligocyclizations of open-chain substrates, containing several multiple bond fragments, under Heck-type reaction[3] and cycloisomerization conditions[4,5] have been among the most extensively studied processes in this area.

As has previously been reported by our own group,[6] different 2-bromodienyne substrates of the general type **1** can undergo mainly two modes of palladium-catalyzed cascade oligocyclizations to furnish either tricyclic bisannelated cyclohexadiene derivatives of type **2** or tetracyclic skeletons of type **3** with a bridge-annelated cyclopropane moiety between rings A and B ring (Scheme 1).



Scheme 1. Two modes of palladium-catalyzed intramolecular oligocyclizations of 2-bromodienynes.

In addition, more recently we disclosed[7] that the mechanistic pathways and hence the outcomes of the palladium-catalyzed cascade oligocyclizations of 2-bromoalk-1-ene-(*n*+1),(*m*+*n*+1)-diynes can be determined by the tether lengths between each two pairs of multiple bond fragments and the nature of the substituent at the acetylene terminus.

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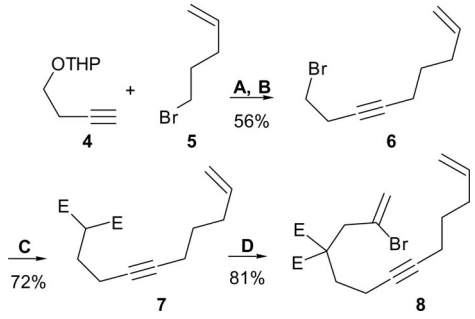
The current study, accordingly, has been conducted to explore the effect of the tether lengths and the nature of the terminal substituents on determining the modes of palladium-catalyzed cascade oligocyclizations of 2-bromoalka-1,(*n*+*m*+1)-diene-(*n*+1)-ynes.[8]

Results and Discussion

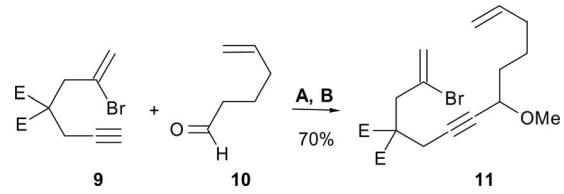
Preparation of the Oligocyclization Substrates

Substrates containing a three-atom and a four-atom tether between the vinyl bromide moiety as well as the terminal alkene and the internal acetylene were prepared by deprotonating tetrahydropyranyl-protected but-3-yn-1-ol (**4**) at –78 °C with *n*-butyllithium and treating the resulting lithium acetylide with 5-bromo-1-pentene (**5**) to furnish 2-(8′-nonen-3′-ynyloxy)tetrahydro-2*H*-pyran. Following a published procedure,[9] the tetrahydropyranyloxy group was directly converted into a bromine substituent by treating the acetal at –20 °C in dichloromethane with triphenylphosphane and bromine to give 9-bromo-1-nonen-6-yne (**6**) in 56% yield over both steps from **4**. The bromoenyne **6** was then used to alkylate diethyl malonate enolate at ambient temperature in dimethylformamide (DMF) to produce diethyl 2-(8′-nonen-3′-ynyl)malonate (**7**) in 72% yield. The sodium enolate of **7** was subsequently allylated with 2,3-dibromopropene in dimethoxyethane (DME), which turned out to provide a higher yield (81%) of the desired diethyl 2-bromotrideca-1,12-dien-7-yne-4,4-dicarboxylate (**8**) than when working in dimethylformamide (DMF) (Scheme 2).



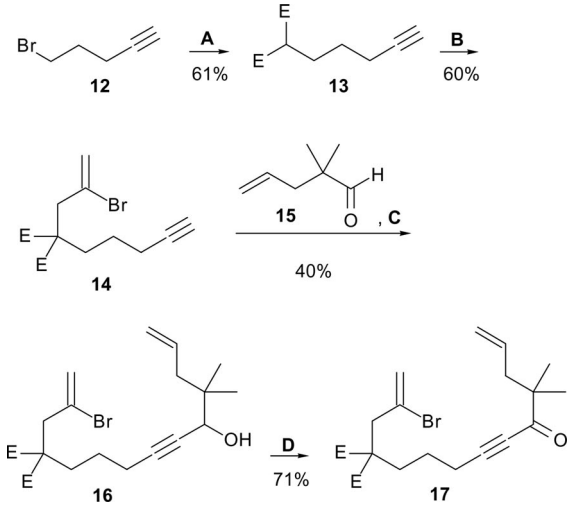
Scheme 2. Synthesis of diethyl 2-bromotrideca-1,12-dien-7-yne-4,4-dicarboxylate with a four- and a three-atom tether connecting the vinyl bromide and the terminal alkene moiety, respectively, with the internal acetylene. **A**: 1) *n*BuLi, THF, –78 °C, 10 min 2) 5-bromo-1-pentene (**2**), HMPA, –78 °C→ room temp., 24 h; **B**: PPh_3, Br_2, CH_2Cl_2, –20 °C→ room temp., 24 h. **C**: NaH, dimethyl malonate, DMF, room temp., 24 h, **D**: NaH, 2,3-dibromopropene, DME, room temp., 12 h (E = CO_2Me).

Another substrate with a four- and a three-atom tether between each pair of multiple bonds, but in reverse order than **8**, was also prepared. Deprotonation of the previously described diethyl 2-(2′-bromoallyl)-2-(2′′-propynyl)malonate (**9**)[6d] at –78 °C with *n*-butyllithium, subsequent addition of the resulting lithium acetylide to the carbonyl group of 5-hexenal (**10**) and in situ methylation of the newly generated propargyl alkoxide with methyl iodide furnished diethyl 2-bromo-8-methoxytrideca-1,12-dien-6-yne-4,4-dicarboxylate (**11**) in 70% overall yield from **9** (Scheme 3).



Scheme 3. Synthesis of diethyl 2-bromo-8-methoxytrideca-1,12-dien-6-yne-4,4-dicarboxylate with a three- and a four-atom tether between the vinyl bromide as well as the terminal alkene moiety, respectively, and the internal acetylene. **A**: 1) *n*BuLi, THF, –78 °C, 10 min, 2) 5-hexenal (**7**), –78→0 °C, 30 min; **B**: MeI, DMSO, 0 °C, 2 h (E = CO_2Et).

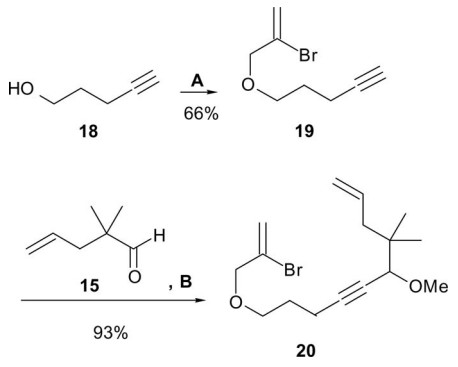
A cyclization precursor with a five- and a three-atom tether between each pair of multiple bonds was prepared by alkylating sodium diethyl malonate enolate with 5-bromopentyne (**12**) to produce diethyl 2-(5-pentynyl)malonate (**13**). The sodium enolate of the latter was allylated with 2,3-dibromopropene to afford the 2-bromonon-1-en-8-yne derivative **14**. The enyne **14** was then deprotonated at –78 °C with *n*-butyllithium, and the resulting lithium acetylide was added to the carbonyl group of 2,2-dimethyl-4-pentenal (**15**)[10] to provide the propargyl alcohol **16** which, upon Swern oxidation, furnished diethyl 2-bromo-11,11-dimethyl-10-oxotetradeca-1,13-dien-8-yne-4,4-dicarboxylate (**17**) in 72% yield (Scheme 4).



Scheme 4. Synthesis of diethyl 2-bromo-10-methoxytetradeca-1,13-dien-8-yne-4,4-dicarboxylate with a five- and a three-atom tether between the vinyl bromide as well as the terminal alkene moiety, respectively, and the internal acetylene. **A**: diethyl malonate, NaH, DMF, room temp., 2 d; **B**: 1) NaH, DME 2) 2,3-dibromopropene, room temp., 2 h; **C**: 1) *n*BuLi, THF, –78 °C, 10 min, 2) 2,2-dimethyl-4-pentenal (**15**), –78→20 °C, 30 min; **D**: $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, –60→20 °C (E = CO_2Et).

An additional substrate with a five- and a three-atom tether, but with an oxygen atom in the former, was prepared in a similar way. Following a published procedure,[11] 4-pentynol (**18**) was converted into the ether **19** with 2,3-dibro-

mopropene at ambient temperature in dichloromethane/water employing sodium hydroxide and cetyltrimethylammonium bromide (CETAB) as a phase-transfer catalyst. The resulting 5-(2′-bromoallyloxy)pent-1-yne (**19**) was subjected to the same sequence of reactions as for the preparation of **17** from the enyne **14**, to furnish the targeted 10-(2′-bromoallyloxy)-5-methoxy-4,4-dimethyl-1-decen-6-yne (**20**) in 93% overall yield (Scheme 5).



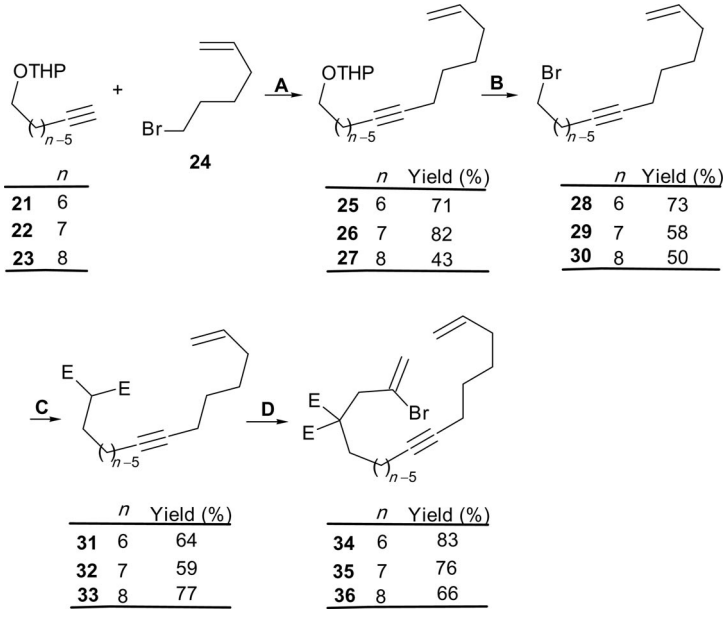
Scheme 5. Synthesis of 10-(2′-bromoallyloxy)-5-methoxy-4,4-dimethyl-1-decen-6-yne (**20**) with an oxygen-containing five-atom tether. **A**: 2,3-dibromopropene, NaOH, CETAB, H_2O, CH_2Cl_2, 20 °C, 6 h; **B**: 1) *n*BuLi, THF, –78 °C, 10 min, 2) 2,2-dimethyl-4-pentenal (**15**), –78→20 °C, 30 min, 3) MeI, DMSO, 0 °C, 2 h.

Three cyclization precursors, all with a tetramethylene chain between the terminal alkene and the internal acetylene, but with four-, five- and six-atom tethers connecting the vinyl bromide moiety and the internal alkyne, were accessed via the tetrahydropyranyl-protected alk-1-en-7-yn-(*n*+4)-ols **25**–**27** obtained by alkylating the lithium acetylides, generated from the tetrahydropyranyloxyalkynes **21**–**23** by deprotonation with *n*-butyllithium at –78 °C, with 6-bromo-1-hexene (**24**) in 71, 82, and 43% yield, respectively. The tetrahydropyranyloxy groups in **25**–**27** were directly converted into bromine substituents, and the resulting alkenynyl bromides **28**–**30** were used to alkylate sodium diethyl malonate enolate to provide **31**, **32**, and **33** in 64, 59, 77% yield, respectively. The latter were allylated with 2,3-dibromopropene to furnish the desired diethyl 2-bromoalka-1,(*n*+7)-dien-(*n*+1)-yne-4,4-dicarboxylates **34**, **35**, and **36** in 83, 76, and 66% yield, respectively (Scheme 6).

Palladium-Catalyzed Oligocyclizations

When substrates each with one three- and one four-atom tether **8** and **11**, respectively, were treated in acetonitrile at 80 °C with palladium acetate (5–10 mol-%), triphenylphosphane (10–25 mol-%), and silver carbonate (3 equiv.) for 16–34 hours, all the starting material was consumed and the tricyclic compounds **37** and **39** with one five- and one six-membered ring annelated to a central cyclohexadiene moiety were isolated in 30 and 37% yield, respectively; in addition to **37**, the aromatic product **38** (18% yield), resulting from dehydrogenation of **37**, was formed (Scheme 7).

The dienynes **17** and **20**, each with a five- and a three-atom tether, under similar conditions also led to the consumption of all the starting material and gave the bisannelated cyclohexadienes **40** (33%) and **41** (43%), respectively, along with the dehydrogenation product **42** (5%) in the latter case (Scheme 8). However, these transformations required rather long reaction times, namely 4 days in the case of **17** in acetonitrile and 10 days in the case of **20** in DMF.



	n
21	6
22	7
23	8

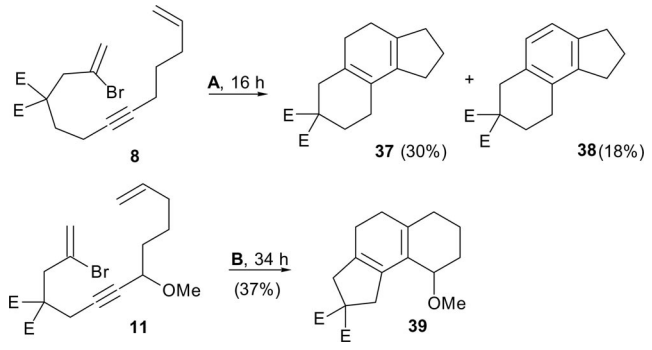
	n	Yield (%)
25	6	71
26	7	82
27	8	43

	n	Yield (%)
28	6	73
29	7	58
30	8	50

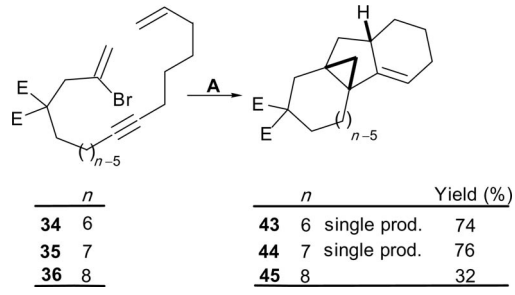
	n	Yield (%)
31	6	64
32	7	59
33	8	77

	n	Yield (%)
34	6	83
35	7	76
36	8	66

Scheme 6. Synthesis of diethyl 2-bromoalka-1,(*n*+7)-dien-(*n*+1)-yn-4,4-dicarboxylates each with a tetramethylene linker between the terminal alkene and the internal alkyne unit and a four-, five-, and six-atom tether between the vinyl bromide and the internal acetylene. **A**: 1) *n*BuLi, THF, –78 °C, 10 min, 2) 6-bromo-1-hexene (**21**), HMPA, –78 °C→ room temp., 24 h; **B**: PPh_3, Br_2, CH_2Cl_2, –20 °C→ room temp., 24 h. **C**: NaH, diethyl malonate, DMF, room temp., 24 h, **D**: NaH, 2,3-dibromopropene, DME, room temp., 4 h (E = CO_2Et).



Scheme 7. Palladium-catalyzed oligocyclizations of diethyl 2-bromotrideca-1,12-dien-*n*-yn-4,4-dicarboxylates (**8**, *n* = 7) and (**11**, *n* = 6) with one three- and one four-atom tether. **A**: $Pd(OAc)_2$ (10 mol-%), PPh_3 (25 mol-%), Ag_2CO_3 (3 equiv.), MeCN, 80 °C; **B**: $Pd(OAc)_2$ (5 mol-%), PPh_3 (10 mol-%), Ag_2CO_3 (3 equiv.), MeCN, 80 °C (E = CO_2Me).



	n
34	6
35	7
36	8

	n		Yield (%)
43	6	single prod.	74
44	7	single prod.	76
45	8		32

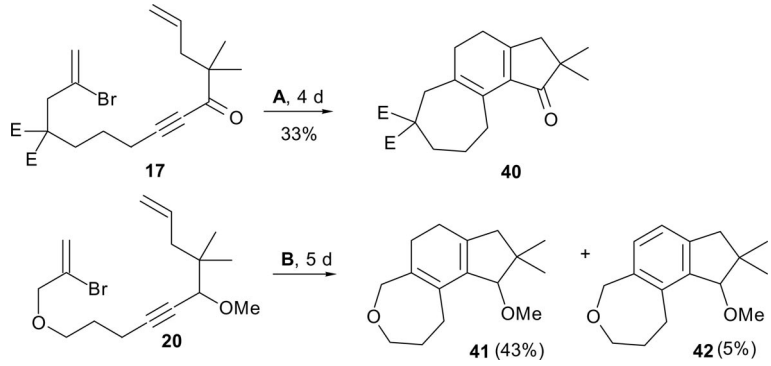
Scheme 9. Palladium-catalyzed oligocyclizations of diethyl 2-bromoalka-1,(*n*+7)-dien-(*n*+1)-yne-4,4-dicarboxylates with a four-, five-, and six-atom tether between the vinyl bromide moiety and the internal acetylene as well as a tetramethylene linker between the acetylene and the terminal alkene moiety. **A**: $Pd(OAc)_2$ (10 mol-%), PPh_3 (25 mol-%), Ag_2CO_3 (1.5 equiv.), MeCN, 80 °C (E = CO_2Me).

The thus formed tricyclic systems could easily be identified on the basis of their ^{13}C NMR spectra compared to those of the starting materials. The disappearance of the acetylenic carbon signals and the appearance of four new signals of quaternary olefinic carbon atoms provide a strong evidence for the formation of tricyclic systems with two tetrasubstituted double bonds.

Acyclic 2-bromoalka-1,(*n*+7)-dien-(*n*+1)-ynes with more than three atoms in both tethers between each pair of multiple bonds, undergo palladium-catalyzed oligocyclization by a different mode, as evidenced by the transformation of the substrates **34**–**36**. Instead of bisannelated cyclohexadienes, they yield tetracycles with a central five-membered ring and a cyclopropane moiety attached to the bridge between the first formed and this ring. Thus, when **34**–**36**, respectively, were treated with a palladium precatalyst system typically employed for Heck reactions [$Pd(OAc)_2$ (10 mol-%), PPh_3 (25 mol-%), Ag_2CO_3 (1.5 equiv.), MeCN], compounds **43**, **44**, and **45** were isolated in 74, 76 and 32% yield, respectively (Scheme 9).

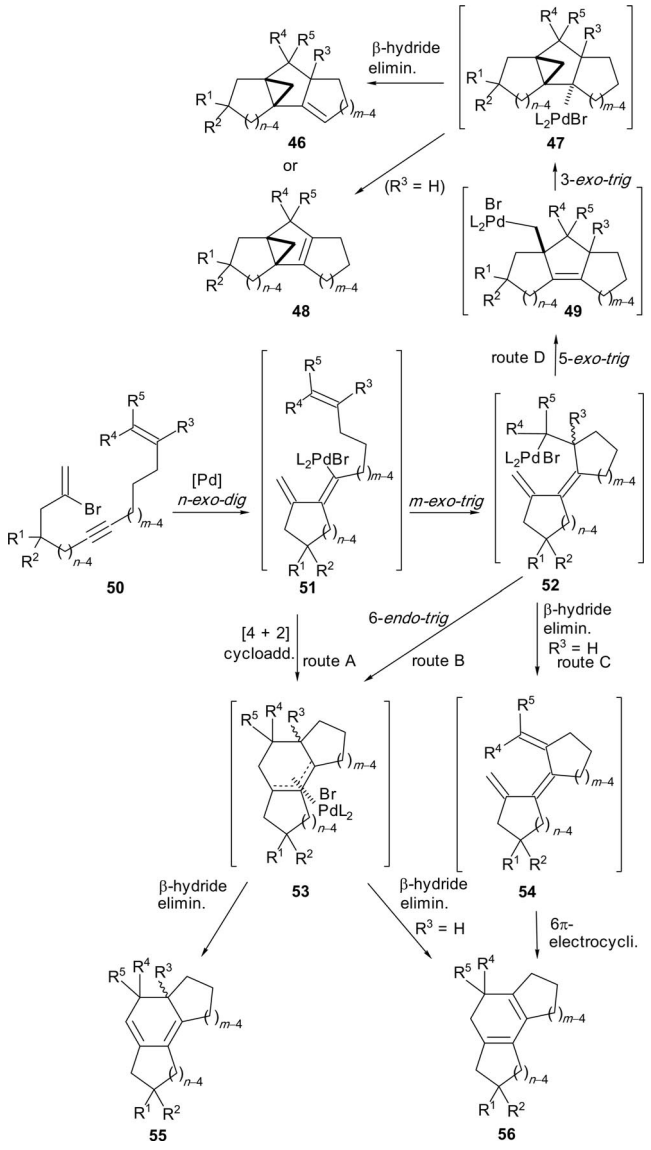
Discussion

All the palladium-catalyzed cascade oligocyclizations of 2-bromoalka-1,(*n*+*m*+1)-dien-(*n*+1)-ynes **50** are triggered by an oxidative addition of the vinyl bromide moiety to an in situ produced Pd^0 species. This will be followed by an *n-exo-dig* carbopalladation of the triple bond to provide a dienylpalladium bromide **51** with a tethered alkenyl side chain. This intermediate may undergo either an intramolecular [4+2] cycloaddition with subsequent dehydropalladation to produce the tricyclic systems **55** and **56** via the tricyclic π-allylpalladium intermediate **53** (Scheme 10, route A). The latter can also arise from 6-*endo-trig* carbopalladation in the σ-alkylpalladium intermediate **52** (route B), which would be formed by *m-exo-trig* carbopalladation in **51**. The intermediate **52** can also undergo β-hydride elimination to furnish the bicyclic 1,3,5-hexatriene **54**, which subsequently yields the tricyclic diene **56** by 6π-electrocyclization (Scheme 10, route C). The ultimate possible reaction mode for the intermediate **52** is to undergo a further 5-*exo-trig* carbopalladation to yield the neopentyl-type σ-alkylpalladium species **49** which has no choice but to perform a 3-*exo-trig* carbopalladation to furnish the tetracyclic σ-



Scheme 8. Palladium-catalyzed oligocyclizations of 2-bromo-11,11-dimethyl-10-methoxytetradeca-1,13-dien-8-ynes each with one three- and one five-atom tether. **A**: $Pd(OAc)_2$ (10 mol-%),PPh_3 (25 mol-%), Ag_2CO_3 (1.5 equiv.), MeCN, 80 °C; **B**: $Pd(OAc)_2$ (10 mol-%), PPh_3 (25 mol-%), Ag_2CO_3 (3 equiv.), DMF, 80 °C (E = CO_2Me).

alkylpalladium complex **47** which, by β-hydride elimination, eventually yields the cyclopropane-bridged tetracycles **46** and/or **48**, depending on whether the bridgehead substituent R^3 is an alkyl group or a hydrogen atom (Scheme 10, route D).



Scheme 10. Possible pathways for cascade oligocyclizations of 2-bromoalka-1,(*n*+*m*+1)-diene-(*n*+1)-ynes (**50**). *n* = 5, 6, 7,and 8; *m* = 5 or 6.

The formation of tetracyclic products such as **46** and **48** from the appropriate precursors indicates that the third carbopalladation step, when it occurs, prefers the 5-*exo-trig* rather than the 6-*endo-trig* mode. In addition, the intramolecular [4+2] cycloaddition in **51** (route A, Scheme 10) apparently is not a favored route, unless the non-brominated terminal vinyl moiety bears an activating electron-withdrawing group.[6d]

As has been reported recently,[7] the square-planar intermediate σ-alkylpalladium complex **52** arising after the second carbopalladation step, must be in a non-coplanar orientation with respect to the exomethylene group on the first formed ring in order for it to coordinate and eventually insert into this group. This situation turns up when the intermediate of type **52** comprises two six-membered rings. However, a σ-alkylpalladium intermediate of type **52** with at least one five-membered ring arising from a three-atom tether will be nearly coplanar with respect to the exomethylene group and, hence, it will not be in a suitable orientation to coordinate and to insert into this group (Scheme 10, route C).

Accordingly, the preferred conformation of the intermediates of type **52** comprising one five- and one six- (*n* = 5, *m* = 6), (*n* = 6, *m* = 5) or even seven-membered ring (*n* = 7, *m* = 5) will be dominated by the geometry of the five-membered ring and the plane of the square-planar σ-alkylpalladium complex will be nearly coplanar to the exomethylene group (Figure 1). Consequently, products **37**, **39**, **40** and **41** from the corresponding acyclic precursors **8**, **11**, **17** and **20** also arise by two cyclizing carbopalladations to furnish the intermediates of type **52** which preferably undergo dehydropalladation and ensuing 6π-electrocyclization.

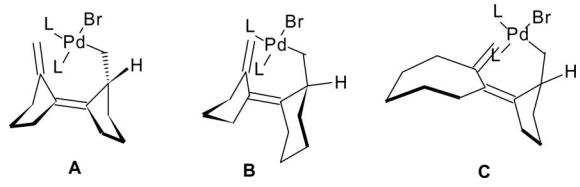


Figure 1. Optimized conformations of the intermediates of type **52** containing at least one five-membered ring.

On the other hand, the preferred conformation of intermediates of type **52** comprising one six- and a second six- (*n* = 6, *m* = 6), a seven- (*n* = 7, *m* = 6) or even an eight-membered ring (*n* = 8, *m* = 6) will put the square-planar σ-alkylpalladium fragment in a suitable position to coordinate the exomethylene group (Figure 2) and insert into it in a 5-*exo-trig* mode (Scheme 10, route D). Therefore, bromodienynes **34**, **35**, and **36** all undergo cascade transformations via **52** along route D (Scheme 10) to provide tetracyclic products **43**, **44** and **45**, respectively.

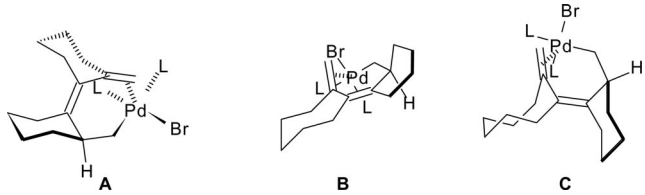


Figure 2. Optimized conformations of the intermediates of type **52** containing one six-membered ring and a second six-membered or one six-membered and one larger ring.

Conclusions

This study complements the previously initiated systematic variation of substituents and tether lengths in 2-bromoalka-1,(*n*+*m*+1)-dien-(*n*+1)-ynes and their effect on the outcome of the palladium-catalyzed cascade oligocycliza-

tions. The results contribute to a further understanding of the various reaction modes. This helps to make such transformations predictable and thus applicable in the synthesis of multifunctional molecules with the desired skeletons.

Experimental Section

General Remarks: ^{1}H NMR spectra were recorded on Bruker AM 250 (250 MHz), and AX 300 (300 MHz) instruments at ambient temperature for $CDCl_3$ or C_6D_6 solutions 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), bs (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), m_c (centered multiplet). ^{13}C NMR spectra were recorded on a Bruker AM 250 (62.5 MHz) instrument at ambient temperature for $CDCl_3$ solutions, with δ ($CDCl_3$) = 77.0 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 DEPT (Distortionless Enhancement by Polarization Transfer) measurements and are designated as follows: CH_3, CH = (+), CH_2 = (–), quaternary C = (C_{quat}). 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 Silica Gel 60 (0.063–0.200 mm). Thin layer chromatography: Macherey–Nagel Alugram G/UV_{254} 0.25 mm silica gel-coated sheets 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, Et_2O = diethyl ether, HMPA = hexamethylphosphorictriamide, DMF = dimethylformamide, PE = light petroleum, b.p. 40–50 °C.

General Procedure for Alkylating Alkynes with Alkyl Bromides (GP1): To a solution of the respective alkyne (22.0 mmol) in THF (50 mL) was added dropwise at –78 °C *n*-butyllithium (24.0 mmol, hexane solution). After stirring at this temperature for 30 min, the respective alkyl bromide (22.0 mmol) and HMPA (4.40 mL, 25 mmol) were added, and stirring was continued at –78 °C for 1 h and then at ambient temperature for 6 h. The reaction mixture was then diluted with water (50 mL) and the mixture extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography.

General Procedure for Alkylating Dialkyl Malonates with Alkyl Bromides (GP2): The dialkyl malonate (55.0 mmol) was added dropwise at room temperature to a suspension of sodium hydride (1.44 g, 60 mmol, oil suspension) in DME, DMF, or DMSO (150 mL). The resulting clear solution was then transferred into a solution of the respective alkyl halide (55.0 mmol) in DME, DMF, or DMSO (20 mL). After stirring from 2 h to 2 d, the reaction mixture was diluted with water (100 mL) and the mixture extracted with diethyl ether (2 × 50 mL). The combined organic layers were dried ($MgSO_4$), concentrated and the residue was purified by column chromatography.

General Procedure for Converting a Tetrahydropyranyloxy Group Into a Bromine Substituent (GP3):[9] Bromine (60 mmol) was added dropwise at –20 °C to a solution of triphenylphosphane (60 mmol) in dichloromethane (150 mL). After stirring at –20 °C for 30 min, the respective tetrahydropyranyl ether (27.0 mmol) was added to the colorless suspension of the triphenylphosphane–bromine complex, and stirring was continued at ambient temperature for 20 h. Water was then poured into the reaction mixture, the two layers were separated, and the aqueous layer was extracted with dichloromethane (100 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the resulting residue was purified by column chromatography.

General Procedure for Coupling a 2-Bromoalkenyne with an Aldehyde (GP4): To a solution of the respective 2-bromoalkenyne (1.0 mmol) in THF (15 mL) was added dropwise at –78 °C *n*-butyllithium (24.0 mmol, hexane solution). After stirring for 30 min, the respective aldehyde (1.05 mmol) was added, and stirring was continued at –78 °C for 30 min. After warming the mixture to –10 °C, methyl iodide (1 mmol) and DMSO (10 mL) were added, and stirring was continued at 0 °C for 2 h. The reaction mixture was then diluted with water (20 mL), the two layers were separated, and the aqueous layer was extracted with diethyl ether (2 × 30 mL). The combined organic layers were washed with conc. sodium chloride solution (20 mL), dried ($MgSO_4$), and concentrated. The resulting residue was purified by column chromatography.

9-Bromo-1-nonen-6-yne (6): The preparation of 2-(8′-nonen-3′-ynyloxy)tetrahydro-2*H*-pyran from **5** and **4** with the use of sodium amide in liquid ammonia and DMSO has been reported in the literature.[12] Alternatively, it can be prepared according to GP(1) by adding dropwise at –78 °C, *n*-butyllithium (26.3 mL, 42.0 mmol, 1.6 M in hexane) to a solution of 2-(3′-butynyloxy)tetrahydro-2*H*-pyran (**4**) (6.16 g, 40 mmol) in THF (80 mL). After stirring for 30 min, 5-bromo-1-pentene (**5**) (5.96 g, 40 mmol) and HMPA (7.9 mL) were added, and stirring was continued at –78 °C for 30 min and at ambient temperature for 6 h. Work-up provided 8.90 g (100%) of 2-(8′-nonen-3′-ynyloxy)tetrahydro-2*H*-pyran as a colorless liquid. Without any further purification, the latter compound (8.90 g, 40 mmol) was added at –20 °C to a colorless suspension of triphenylphosphane–bromine complex formed by adding dropwise at –20 °C bromine (16.0 g, 100 mmol) to a solution of triphenylphosphane (26.2 g, 100 mmol) in dichloromethane (240 mL). After stirring at ambient temperature for 20 h, work-up as described in GP3, the resulting residue was purified by column chromatography (250 g of silica gel, column 6 × 60 cm, pentane) to afford 4.52 g (56%) of **6** as a colorless liquid. R_f (PE) = 0.48. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.61 (tt, ^3J = 7.3, ^3J = 7.3 Hz, 2 H,4-H), 2.16 [m, 4 H, 3(5)-H], 2.71 (tt, ^3J = 7.3, ^5J = 2.3 Hz, 2 H, 8-H), 3.41 (t, ^3J = 7.3 Hz, 2 H, 9-H), 4.99 (dt, ^3J = 10.1, ^4J = 1.0 Hz, 1 H, 1-H), 5.06 (dt, ^3J = 17.5, ^4J = 1.5 Hz, 1 H, 1-H), 5.77 (m, 1 H, 2-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.03 (C-5), 23.29 (C-8), 27.89 (C-4), 30.37 (C-9), 32.69 (C-3), 77.17 (C-6), 82.18 (C-7), 115.08 (C-1), 137.86 (C-2) ppm.

Dimethyl 2-(8′-Nonen-3′-ynyl)malonate (7): Following GP2, dimethyl malonate (2.64 g, 20 mmol) was added dropwise at room temperature to a mixture of sodium hydride (0.88 g, 22 mmol, 60% oil suspension) and anhydrous DMF (50 mL). The resulting clear solution was transferred into a solution of 9-bromo-1-nonen-6-yne (**6**) (3.71 g, 18.5 mmol) in DMF (20 mL). After stirring for 2 d and

work-up, the residue was purified by column chromatography (80 g of silica gel, column 2.5 × 40 cm, PE/Et_2O, 15:1) to afford 3.35 g (72%) of **7** as a colorless oil. R_f (PE/Et_2O, 15:1) = 0.25. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.54 (tt, ^3J = 7.2, ^3J = 7.2 Hz, 2 H, 6′-H), 2.00–2.25 [m, 8 H, 1′(2′,5′,7′)-H], 3.60 (t, ^3J = 7.4 Hz, 1 H, 2-H), 3.72 (s, 6 H, OCH_3), 4.93 (dt, ^3J = 10.1, ^4J = 1.0 Hz, 1 H, 9′-H), 5.00 (dt, ^3J = 17.2, ^4J = 1.4 Hz, 1 H, 9′-H), 5.76 (m_c, 1 H, 8′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 16.68 (C-2′), 18.02 (C-5′), 27.99 (C-6′*), 28.03 (C-1′*), 32.71 (C-7′), 50.20 (C-2), 52.51 (2 OCH_3), 78.03 (C-3′**), 81.45 (C-4′**), 114.98 (C-9′), 137.91 (C-8′), 169.54 (2 C=O) ppm. MS (DCI, NH_3): *m*/*z* (%) = 522 (100) [2M + NH_4^+], 270 (10) [M + NH_4^+], 235 (18).

Dimethyl 2-Bromotrideca-1,12-diene-7-yne-4,4-dicarboxylate (8): Following GP2, to a suspension of sodium hydride (0.6 g, 15 mmol, 60% oil suspension) in DME (25 mL) was added dropwise at room temperature dimethyl 2-(8′-nonen-3′-ynyl)malonate (**7**) (3.35 g, 13.3 mmol). After stirring for 30 min, 2,3-dibromopropene (3.0 g, 15.0 mmol) was added, and stirring was continued for 12 h. After work-up, the residue was purified by column chromatography (80 g of flash silica gel, column 2.5 × 40 cm, PE/Et_2O, 15:1) to afford 4.0 g (81%) of **8** as a colorless oil. R_f (PE/Et_2O, 15:1) = 0.29. IR (film): $\tilde{\nu}$ = 3076 , 2950 (CH), 2842, 1737 (C=O), 1641, 1625 (C=C), 1277, 1245, 1212, 1154, 1085, 1015, 913 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.40 (tt, ^3J = 7.2, ^3J = 7.2 Hz, 2 H, 10-H), 2.05–2.14 [m, 8 H, 5(6,9,11)-H], 3.15 (s, 2 H, 3-H), 3.71 (s, 6 H, OCH_3), 4.95 (dt, ^3J = 10.3, ^4J = 1.0 Hz, 1 H, 13-H), 4.99 (dt, ^3J = 17.1, ^4J = 1.5 Hz, 1 H, 13-H), 5.57 (d, ^2J = 1.6 Hz, 1 H, 1-H), 5.67 (d, ^2J = 1.6 Hz, 1 H, 1-H), 5.76 (m_c, 1 H, 12-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.25 (–, C-6), 18.12 (–, C-9), 28.01 (–, C-10), 31.13 (–, C-5), 32.77 (–, C-11), 43.16 (–, C-3), 52.72 (+, 2 OCH_3), 56.42 (C_{quat}, C-4), 78.52 (C_{quat}, C-7*), 80.63 (C_{quat}, C-8*), 115.00 (–, C-13), 122.06 (–, C-1),126.82 (C_{quat}, C-2), 137.94 (+, C-12), 170.53 (C_{quat}, 2 C=O) ppm. MS (DCI, NH_3): *m*/*z* = 391/390/389/388 (18:100:18:91) [M + NH_4^+]. $C_{17}H_{23}BrO_4$ (371.3): calcd. C 55.00, H 6.24; found C 55.25, H 6.32.

Diethyl 2-Bromo-8-methoxytrideca-1,12-dien-6-yne-4,4-dicarboxylate (11): Following GP4, *n*-butyllithium (0.53 mL, 1.0 mmol, 1.88 M in hexane) was added dropwise at –78 °C to a solution of 2-(2′-bromoallyl)-2-(3′′-propynyl)malonate (**9**)[6d] (317 mg, 1 mmol) in THF (15 mL). After stirring at –78 °C for 30 min, 5-hexenal (98 mg, 1.0 mmol) was added, and stirring was continued at this temperature for 30 min. The reaction mixture was warmed to –10 °C and methyl iodide (142 mg, 1 mmol) as well as DMSO (10 mL) were added. After stirring at 0 °C for 2 h and work-up, the residue was purified by column chromatography (20 g of silica gel, column 1.5 × 20 cm, PE/Et_2O, 10:1) to furnish 300 mg (70%) of **11** as a colorless oil. IR (film): $\tilde{\nu}$ = 3074 , 2980, 2921, 1736, 1430, 1289, 1216, 1110, 1045, 900, 619 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.50 (m, 2 H, 10-H), 1.62 (m, 2 H, 9-H), 2.04 (dt, ^3J = 7.0, ^3J = 7.0 Hz, 2 H, 11-H), 2.96 (d, ^5J = 1.8 Hz, 2 H, 5-H), 3.26 (s, 2 H, 3-H), 3.32 (s, 3 H,OCH_3), 3.89 (m, 1 H, 8-H), 4.21 (m, 4 H, OCH_2CH_3), 4.93 (dd, ^3J = 10.1, ^2J = 1.9 Hz, 1 H, 13-H), 5.00 (dd, ^3J = 17.0, ^2J = 2.0 Hz, 1 H, 13-H), 5.59 (d, ^2J = 1.4 Hz, 1 H, 1-H), 5.79 (d, ^2J = 1.4 Hz, 1 H, 1-H), 5.82 (m, 1 H, 12-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.88 (+, 2 OCH_2CH_3), 22.45 (–, C-5), 24.42 (–, C-10), 33.30 (–, C-11), 35.16 (–, C-9), 42.79 (–, C-3), 56.14 (C_{quat}, C-4), 56.17 (+, OCH_3), 61.83 (–, 2 OCH_2), 71.05 (+, C-8), 80.47 (C_{quat},C-6*), 82.74 (C_{quat}, C-7*), 114.63 (–, C-13), 122.30 (–, C-1), 126.57 (C_{quat},C-2), 138.34 (+, C-12), 169.03 (C_{quat}, 2 C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 349 (100) [M^+ – Br], 327 (13), 285 (22), 243 (59), 206 (17), 178 (21), 119 (36), 91 (30), 81 (22), 55 (13), 41 (16).

Diethyl 2-(4′-Pentynyl)malonate (13):[13] Following GP2, diethyl malonate (8.0 g, 50 mmol) was added dropwise at room temperature to a solution of sodium hydride (2.2 g, 55 mmol, 60% oil suspension) in anhydrous DMSO (100 mL). The resulting clear solution was transferred into a solution of 5-bromo-1-pentyne (7.35 g, 50 mmol) in DMSO (20 mL). After stirring for 2 d and work-up, the resulting residue was purified by column chromatography (150 g of silica gel, column 5 × 40 cm, PE/Et_2O, 15:1) to afford 6.89 g (61%) of **13** as a colorless liquid. R_f (PE/Et_2O, 10:1) = 0.31. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.53 (m_c, 2 H, 2′-H), 1.97 [m, 3 H, 1′(5′)-H], 2.16 (dt, ^3J = 7.0, ^4J = 2.6 Hz, 2 H, 3′-H), 3.42 (t, ^3J = 7.0 Hz, 1 H, 2-H), 4.18 (m, 4 H, OCH_2) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.98 (OCH_3CH_3), 18.05 (C-3′), 26.03 (CH_2), 27.65 (CH_2), 51.45 (C-2), 61.30 (OCH_2), 68.82 (C-5′), 83.35 (C-4′), 169.16 (C=O) ppm.

Diethyl 2-(2′-Bromoallyl)-2-(4′′-pentynyl)malonate (14): Following GP2, to a suspension of sodium hydride (0.88 g, 22 mmol, 60% oil suspension) in DME (40 mL) was added dropwise at room temperature diethyl 2-(4′-pentynyl)malonate (**13**) (4.51 g, 20.0 mmol). After stirring for 30 min, 2,3-dibromopropene (4.40 g, 22.0 mmol) was added, and stirring was continued for 2 h. After work-up, the residue was purified by column chromatography (80 g of silica gel, column 2.5 × 50 cm, PE/Et_2O, 20:1) to afford 4.06 g (60%) of **14** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.35. IR (film): $\tilde{\nu}$ = 3288 (alkyne), 2980 (CH), 1732 (C=O), 1626 (C=C), 1446, 1368, 1278, 1181, 1095, 1026, 902, 858, 643 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.40 (m, 2 H, 2′′-H), 1.93 (t, ^4J = 2.6 Hz, 1 H, 5′′-H), 2.08 (m, 2 H, 1′′-H), 2.18 (dt, ^3J = 7.0, ^4J = 2.6 Hz, 2 H, 3′′-H), 3.13 (s, 2 H, 1′-H), 4.17 (m, 4 H, OCH_2), 5.55 (d, ^2J = 1.8 Hz, 1 H, 3′-H), 5.64 (m, 1 H, 3′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.94 (2 OCH_2CH_3), 18.50 (C-3′′), 23.28 (C-2′′), 30.51 (C-1′′), 42.78 (C-1′), 56.68 (C-2), 61.54 (2 OCH_2), 68.76 (C-5′′), 83.46 (C-4′′), 121.73 (C-3′), 127.09 (C-2′), 170.33 (2 C=O) ppm. MS (DCI, NH_3): *m*/*z* (%) = 365/364/363/362 (20:100:20:92) [M + NH_4^+].

Diethyl 2-Bromo-11,11-dimethyl-10-hydroxytetradeca-1,13-dien-8-yne-4,4-dicarboxylate (16): *n*-Butyllithium (3.65 mL, 8.5 mmol, 2.33 M in hexane) was added dropwise at –78 °C to a solution of diethyl 2-(2′-bromoallyl)-2-(4′′-pentynyl)malonate (**14**) (2.76 g, 8.0 mmol) in THF (80 mL). After stirring at –78 °C for 30 min, 2,2-dimethyl-4-pentenal (**15**) (1.01 g, 9.0 mmol) was added, and stirring was continued at this temperature for 30 min. The reaction was then quenched with water (10 mL), and the aqueous layer was extracted with Et_2O (2 × 30 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography (50 g of flash silica gel, column 2.5 × 35 cm, PE/Et_2O, 3:1) to furnish 1.46 g (40%) of **16** as a colorless oil. R_f (PE/Et_2O, 3:1) = 0.23. IR (film): $\tilde{\nu}$ = 2973 (CH), 2934, 1734 (C=O), 1626 (C=C), 1461, 1286, 1236, 1036, 911, 855 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.92 (s, 3 H, 11-CH_3), 0.94 (s, 3 H, 11-CH_3), 1.24 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.40 (m, 2 H, 6-H), 1.82 (br. s, 1 H, OH), 2.09 [m, 4 H, 5(12)-H], 2.24 (dt, ^3J = 6.9, ^5J = 1.9 Hz, 2 H, 7-H), 3.14 (s, 2 H, 3-H), 4.02 (t, ^5J = 1.8 Hz, 1 H, 10-H), 4.18 (q, ^3J = 7.1 Hz, 4 H, OCH_2), 5.07 (m, 2 H, 14-H), 5.55 (d, ^2J = 1.6 Hz, 1 H, 1-H), 5.64 (d, ^2J = 1.6 Hz, 1 H, 1-H), 5.81 (m_c, 1 H, 13-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.94 (+, 2 OCH_2CH_3), 18.88 (–, C-7), 22.41 (+, 11-CH_3), 22.61 (+, 11-CH_3), 23.47 (–, C-6), 30.81 (–, C-5), 38.61 (C_{quat}, C-11), 42.69 (–, C-3*), 42.97 (–, C-12*), 56.79 (C_{quat}, C-4), 61.56 (–, 2 OCH_2), 70.33 (+, C-10), 80.16 (C_{quat}, C-8), 85.50 (C_{quat}, C-9), 117.50 (–, C-14), 121.67 (–, C-1), 127.20 (C_{quat}, C-2), 135.00 (+, C-13), 170.38 (C_{quat}, 2 C=O) ppm. MS (DCI, NH_3): *m*/*z* (%) = 477/476/475/474 (23:100:24:98) [M + NH_4^+].

Diethyl 2-Bromo-11,11-dimethyl-10-oxotetradeca-1,13-dien-8-yne-4,4-dicarboxylate (17): DMSO (0.56 g, 7.17 mmol) was added dropwise at –60 °C to a solution of oxalyl chloride (0.46 g, 3.62 mmol) in dichloromethane (10 mL). After stirring for 20 min, diethyl 2-bromo-11,11-dimethyl-10-hydroxytetradeca-1,13-dien-8-yne-4,4-dicarboxylate (**16**) (1.46 g, 3.19 mmol) was added slowly, and stirring was continued at this temperature for 30 min. Triethylamine (0.76 g, 7.51 mmol) was added, and the reaction mixture was warmed to room temperature. The mixture was then diluted with water (10 mL), the two phases separated, and the aqueous phase was extracted with dichloromethane (3 × 10 mL). The combined organic phases were washed with ammonium chloride solution (5 mL), sodium chloride solution (5 mL), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (20 g of flash silica gel, column 1.0 × 30 cm, PE/Et_2O, 10:1) to furnish 1.03 g (71%) of **17** as a colorless oil. R_f (PE/Et_2O, 5:1) = 0.31. IR (film): $\tilde{\nu}$ = 2976 (CH), 2206, 1733 (C=O), 1668 (C=O), 1626 (C=C), 1367, 1278, 1180, 1094, 1025, 917 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.14 (s, 6 H, 11-CH_3), 1.24 (t, ^3J = 7.2 Hz, 6 H, OCH_2CH_3), 1.46 (m, 2 H, 6-H), 2.10 (m_c, 2 H, 5-H), 2.31 (d, ^3J = 7.5 Hz, 2 H, 12-H), 2.41 (t, ^3J = 7.0 Hz, 2 H, 7-H), 3.15 (s, 2 H, 3-H), 4.19 (q, ^3J = 7.2 Hz, 4 H, OCH_2), 5.05 (m, 2 H, 14-H), 5.55 (m, 1 H, 1-H), 5.65 (br. s, 1 H, 1-H), 5.70 (m_c, 1 H, 13-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.92 (2 OCH_2CH_3), 19.13 (C-7), 22.66 (C-6), 23.52 (2 × 11-CH_3), 30.77 (C-5), 42.90 (C-3*), 43.47 (C-12*), 47.86 (C-11), 56.67 (C-4), 61.63 (2 OCH_2), 79.26 (C-8), 94.12 (C-9), 118.20 (C-14), 121.82 (C-1), 127.00 (C-2), 133.53 (C-13), 170.17 (2 C=O), 193.41 (C-10) ppm. MS (DCI, NH_3): *m*/*z* (%) = 475/474/473/472 (23:100:22:91) [M + NH_4^+]. $C_{22}H_{31}BrO_5$ (455.4): calcd. C 58.03, H 6.86; found C 58.01, H 7.00.

5-(2′-Bromoallyloxy)-1-pentyne (19): 4-Pentyn-1-ol (**18**) (841 mg, 10.0 mmol), cetyltrimethylammonium bromide (CETAB) (182 mg, 0.5 mmol) and 2,3-dibromopropene (2.0 g, 10.0 mmol) were added at ambient temperature to a two-phase mixture of dichloromethane (15 mL) and aq. sodium hydroxide solution (50%, 15 mL). After stirring vigorously at ambient temperature for 6 h, the reaction mixture was diluted with water (50 mL) as well as dichloromethane (50 mL), and the two layers were separated. The aqueous layer was further extracted with dichloromethane (50 mL), the combined organic layers were washed with sodium chloride solution, dried ($MgSO_4$) and concentrated. The residue (10 mL) was treated with diethyl ether (100 mL), and the separated CETAB was filtered off. The ether was evaporated, and the residue was purified by column chromatography (40 g of silica gel, column 2 × 30 cm, pentane/Et_2O, 40:1) to offer 1.35 g (72%) of **19** as a colorless liquid. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.80 (tt, ^3J = 7, ^3J = 6 Hz, 2 H, 4-H), 1.94 (t, ^4J = 2.7 Hz, 1 H, 1-H), 2.31 (dt, ^3J = 7.1, ^4J = 2.7 Hz, 2 H, 3-H), 3.55 (t, ^3J = 6.1 Hz, 2 H, 5-H), 4.08 (dd, ^4J = 1, ^4J = 1 Hz, 2 H, 1′-H), 5.59 (dt, ^2J = 1.6, ^4J = 0.8 Hz,1 H, 3′-H), 5.90 (d, ^2J = 1.6 Hz, 1 H, 3′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.16 (C-3), 28.46 (C-4), 68.60 (C-5 + C-1′), 74.88 (C-1), 83.69 (C-2), 117.36 (C-2′), 129.56 (C-3′) ppm. MS(70 eV, EI): *m*/*z* (%) = 203 (0.4) [M^+ + H], 201 (0.5) [M^+ – H], 189 (0.8), 187 (0.8), 123 (35),122/121/120/119 (20:93:20:84) [$C_3H_4Br^+$], 97 (53), 95 (56), 81 (56), 67 (59), 53 (44), 41 (100). MS (DCI, NH3): *m*/*z* (%) = 223/222/221/220 (10:95:9:100) [M + NH_4^+].

10-(2′-Bromoallyloxy)-4,4-dimethyl-5-methoxy-1-decen-6-yne (20): Following GP4, *n*-butyllithium (2.79 mL, 6.5 mmol, 2.33 M in hexane) was added dropwise at –78 °C to a solution of 5-(2′-bromoallyloxy)-1-pentyne (**19**) (1.12 g, 6.0 mmol) in THF (50 mL). After stirring at –78 °C for 30 min, 2,2-dimethyl-4-pentenal (**15**) (0.73 g, 6.5 mmol) was added, and stirring was continued at this temperature for 30 min. The reaction mixture was then warmed to 0 °C, methyl iodide (852 mg, 6 mmol) and DMSO (50 mL) were added, and stirring was continued at 0 °C for 2 h. After work-up, the residue was purified by column chromatography (25 g of flash silica gel, column 1.5 × 35 cm, PE/Et_2O, 40:1) to furnish 1.68 g (85%) of **20** as a colorless oil. R_f (PE/Et_2O, 20:1) = 0.27. IR (film): $\tilde{\nu}$ = 3074 , 2929, 1640 (C=C), 1445, 1383, 1327, 1099, 916, 672 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.91 (s, 3 H, 4-CH_3), 0.93 (s, 3 H, 4-CH_3), 1.81 (tt, ^3J = 7, ^3J = 6 Hz, 2 H, 9-H), 2.10 (m, 2 H, 3-H), 2.37 (dt, ^3J = 6.9, ^5J = 1.9 Hz, 2 H, 8-H), 3.36 (s, 3 H, OCH_3), 3.54 (t, ^3J = 6.3 Hz, 2 H, 10-H), 3.56 (m, 1 H, 5-H), 4.07 (dd, ^4J = 1, ^4J = 1 Hz, 2 H, 1′-H), 5.00 (m, 2 H, 1-H), 5.59 (dt, ^2J = 1.6, ^4J = 0.8 Hz, 1 H, 3′-H), 5.77 (m_c, 1 H, 2-H), 5.89 (d, ^2J = 1.6 Hz, 1 H, 3′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 15.49 (–, C-8), 22.73 (+, 4-CH_3), 23.12 (4-CH_3), 28.89 (–, C-9), 38.22 (C_{quat}, C-4), 43.01 (–, C-3), 57.12 (+, OCH_3), 68.83 (–, C-10), 74.93 (–, C-1′), 77.79 (C_{quat}, C-7), 79.25 (+, C-5), 86.29 (C_{quat}, C-6), 117.30 (–, C-3′*), 117.37 (–, C-1*), 129.65 (C_{quat}, C-2′), 135.01 (+, C-2) ppm. MS (70 eV, EI): *m*/*z* (%) = 316/315/314/313 (0.2:1:0.2:1) [M^+ – CH_3], 248/247/246/245 (2:20:2:22), 209 (15) [M^+ – C_3H_4Br], 177 (24), 134 (22), 127 (27), 109 (60), 105 (57), 79 (68), 55 (96), 41 (100). MS (DCI, NH_3): *m*/*z* (%) = 349/348/347/346 (15:100:15:97) [M + NH_4^+]. $C_{16}H_{25}BrO_2$ (329.3): calcd. C 58.36, H 7.65; found. C 58.55, H 7.50.

2-(9′-Decen-3′-ynyloxy)tetrahydro-2*H*-pyran (25): Following GP1, to a solution of 2-(3′-butynyloxy)tetrahydro-2*H*-pyran (**21**) (1.54 g, 10.0 mmol) in THF (20 mL) was added dropwise at –78 °C *n*-butyllithium (4.72 mL, 11.0 mmol, 2.33 M in hexane). After stirring at this temperature for 30 min, 6-bromo-1-hexene (**24**) (1.63 g, 10.0 mmol) and HMPA (1.9 mL, 11 mmol) were added, and stirring was continued at –78 °C for 1 h and at ambient temperature for 6 h. After work-up, the residue was purified by column chromatography (60 g of silica gel, column 2.5 × 40 cm, PE/Et_2O, 20:1) to furnish 1.68 g (71%) of **25** as a colorless liquid. R_f (PE/Et_2O, 10:1) = 0.33. IR (film): $\tilde{\nu}$ = 2936 (CH), 1641 (C=C), 1441, 1353, 1261, 1201, 1123, 1082, 1035, 909, 870, 815 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.40–1.92 [m, 10 H, 3 (4, 5, 6′, 7′)-H], 2.05 (m, 2 H, 5′-H), 2.16 (m, 2 H, 8′-H), 2.45 (tt, ^3J = 7.2, ^5J = 2.4 Hz, 2 H, 2′-H), 3.53 (m, 2 H, 6-H), 3.83 (m, 2 H, 1′-H), 4.64 (t, ^3J = 3.1 Hz, 1 H, 2-H), 4.93 (d, ^3J = 10.1 Hz, 1 H, 10′-H), 4.98 (d, ^3J = 17.3 Hz, 1 H, 10′-H), 5.79 (m_c, 1 H, 9′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.56 (C-5′), 19.38 (THP-C), 20.18 (C-2′), 25.40 (THP-C), 27.97 (C-6′*), 28.36 (C-7′*), 30.53 (THP-C), 33.26 (C-8′), 62.13 (C-6), 66.17 (C-1′), 76.90 (C-3′), 81.31 (C-4′), 98.66 (C-2), 114.46 (C-10′), 138.68 (C-9′) ppm. MS (70 eV, EI): *m*/*z* (%) = 235 (0.4) [M^+ – H], 207 (0.3), 193 (0.3), 191 (0.6), 181 (1), 119 (8), 115 (10), 91 (15), 85 (100) [$C_5H_9O^+$], 79 (11), 41 (21).

2-(10′-Undecen-4′-ynyloxy)tetrahydro-2*H*-pyran (26): Following GP1, to a solution of 2-(4′-pentynyloxy)tetrahydro-2*H*-pyran (**22**) (2.27 g, 13.5 mmol) in THF (30 mL) was added dropwise at –78 °C *n*-butyllithium (8.54 mL, 14.0 mmol, 1.64 M in hexane). After stirring at this temperature for 30 min, 6-bromo-1-hexene (**24**) (2.45 g, 15.0 mmol) and HMPA (3.1 mL, 18.0 mmol) were added, and stirring was continued at –78 °C for 1 h and at ambient temperature for 6 h. After work-up, the residue was purified by column chromatography (80 g of silica gel, column 2.5 × 50 cm, PE/Et_2O, 20:1) to furnish 3.54 g (82%) of **26** as a colorless liquid. R_f (PE/Et_2O, 10:1) = 0.33. IR (film): $\tilde{\nu}$ = 2937 , 2866, 1441, 1354, 1138, 1121, 1063, 1035, 992, 909, 816 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.44–1.62 [m, 10 H, 3 (4, 5, 7′, 8′)-H], 1.76 (m, 2 H, 2′-H), 2.04 (m, 2 H, 9′-H), 2.1 (m, 2 H, 6′-H), 2.27 (m, 2 H, 3′-H), 3.48 (m, 2 H, 6-H), 3.82 (m, 2 H, 1′-H), 4.57 (br. s, 1 H, 2-H), 4.93 (d, ^3J = 10.2 Hz, 1 H, 11′-H), 5.00 (d, ^3J = 17.1 Hz, 1 H, 11′-H), 5.80 (m_c, 1 H, 10′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.57 (C-3′),

18.53 (C-6′), 19.44 (THP-C), 25.43 (THP-C), 27.97 (C-7′*), 28.46 (C-8′*), 29.20 (C-2′), 30.61 (THP-C), 33.23 (C-9′), 62.05 (THP-C), 65.97 (C-1′), 79.47 (C-4′**), 80.25 (C-5′**), 98.66 (THP-C), 114.41 (C-11′), 138.67 (C-10′) ppm. MS (70 eV, EI): *m*/*z* (%) = 250 (0.2) [M^+], 249 (0.4) [M^+ – H], 207 (0.5), 167 (8), 97 (8), 85 (100) [$C_5H_9O^+$], 67 (12), 41 (11).

2-(11′-Dodecen-5′-ynyloxy)tetrahydro-2*H*-pyran (27): Following GP1, to a solution of 2-(5′-hexynyloxy)tetrahydro-2*H*-pyran (**23**) (6.38 g, 35.0 mmol) in THF (80 mL) was added dropwise at –78 °C *n*-butyllithium (24.5 mL, 37.0 mmol, 1.51 M in hexane). After stirring at this temperature for 30 min, 6-bromo-1-hexene (**24**) (5.71 g, 35.0 mmol) and HMPA (5.0 mL, 30.0 mmol) were added and stirring was continued at –78 °C for 1 h and at ambient temperature for 6 h. After work-up, the residue was purified by column chromatography (200 g of silica gel, column 5 × 40 cm, PE/Et_2O, 20:1) to furnish 4.0 g (43%) of **27** as a colorless liquid. R_f (PE/Et_2O, 10:1) = 0.38. IR (film): $\tilde{\nu}$ = 2937 (CH), 2864, 1441, 1353, 1138, 1121, 1077, 1035, 991, 908, 869, 815 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.40–1.90 (m, 14 H) 2.00–2.25 [m, 6 H, 4′(7′, 9′)-H], 3.48 (m, 2 H, 6-H), 3.80 (m, 2 H, 1′-H), 4.55 (br. s, 1 H, 2-H), 4.93 (d, ^3J = 10 Hz, 1 H, 12′-H), 5.00 (d, ^3J = 17 Hz, 1 H, 12′-H), 5.80 (m_c, 1 H, 11′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.54 (C-4′, C-7′), 19.56 (THP-C), 25.43 (THP-C), 25.85 (C-3′), 27.98 (C-8′*), 28.48 (C-9′*), 28.85 (C-2′*), 30.67 (THP-C), 33.22 (C-10′), 62.21 (THP-C), 67.00 (C-1′), 79.90 (C-5′**), 80.18 (C-6′**), 98.70 (THP-C), 114.39 (C′-12), 138.68 (C-11′) ppm. MS (DCI, NH_3): *m*/*z* (%) = 282 (45) [M + NH_4^+], 198 (26) [(M – C_5H_8O) + NH_4^+], 102 (100).

10-Bromo-1-decen-7-yne (28): Following GP3, bromine (8.0 g, 50.0 mmol) was added dropwise at –20 °C to a solution of triphenylphosphane (13.1 g, 50.0 mmol) in dichloromethane (120 mL). After stirring at –20 °C for 30 min, 2-(9′-decen-3′-ynyloxy)tetrahydro-2*H*-pyran (**25**) (5.0 g, 21.2 mmol) was added to the colorless suspension of the triphenylphosphane–bromine complex, and stirring was continued at ambient temperature for 20 h. After work-up, the residue was purified by column chromatography (100 g of silica gel, column 2.5 × 60 cm, pentane) to furnish 3.31 g (73%) of **28** as a colorless liquid. R_f (pentane) = 0.49. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.50 [m, 4 H, 4(5)-H], 2.06 (m, 2 H, 3-H), 2.17 (m, 2 H, 6-H), 2.71 (tt, ^3J = 7.4, ^5J = 2.3 Hz, 2 H, 9-H), 3.41 (t, ^3J = 7.4 Hz, 2 H, 10-H), 4.94 (d, ^3J = 10.2 Hz, 1 H, 1-H), 5.01 (d, ^3J = 17.5 Hz, 1 H, 1-H), 5.77 (m, 1 H, 2-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.51 (C-6), 23.32 (C-9), 27.95 (C-4*), 28.18 (C-5*), 30.34 (C-10), 33.21 (C-3), 77.00 (C-8**), 82.40 (C-7**), 114.51 (C-1), 138.61 (C-2) ppm.

11-Bromo-1-undecen-7-yne (29): Following GP3, bromine (5.6 g, 35.0 mmol) was added dropwise at –20 °C to a solution of triphenylphosphane (9.18 g, 35.0 mmol) in dichloromethane (80 mL). After stirring at –20 °C for 30 min, 2-(10′-undecen-4′-ynyloxy)-tetrahydro-2*H*-pyran (**26**) (3.81 g, 15.2 mmol) was added to the colorless suspension of the triphenylphosphane–bromine complex, and stirring was continued at ambient temperature for 20 h. After work-up, the residue was purified by column chromatography (80 g of silica gel, column 2.5 × 40 cm, pentane) to furnish 2.03 g (58%) of **29** as a colorless liquid. R_f (pentane) = 0.49. IR (film): $\tilde{\nu}$ = 3075 , 2930 (CH), 2857, 1641 (C=C), 1434, 1273, 1248, 994, 914, 651 (Br) cm^{-1}. ^1H NMR (250 MHz, CDC_{l3}): δ = 1.48 [m, 4 H, 4(5)-H], 1.99 (tt, ^3J = 7, ^3J = 7 Hz, 2 H, 10-H), 2.05 (m, 2 H, 3-H), 2.14 (tt, ^3J = 6.7, ^5J = 2.4 Hz, 2 H, 6-H), 2.33 (tt, ^3J = 6.8, ^5J = 2.4 Hz, 2 H, 9-H), 3.52 (t, ^3J = 7 Hz, 2 H, 11-H), 4.94 (d, ^3J = 10.1 Hz, 1 H, 1-H), 4.99 (d, ^3J = 17.2 Hz, 1 H, 1-H), 5.80 (m_c, 1 H, 2-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 17.44 (C-9), 18.52 (C-6), 27.99 (C-4*), 28.38 (C-5*), 31.81 (C-10**), 32.61 (C-11**), 33.22 (C-3), 77.97 (C-8), 81.25 (C-7), 114.49 (C-1), 138.64 (C-2) ppm. MS (DCI, NH_3): *m*/*z* (%) = 246 (1) [M + NH_4^+], 166 (19), 109 (100).

12-Bromo-1-dodecen-7-yne (30): Following GP3, bromine (5.6 g, 35.0 mmol) was added dropwise at –20 °C to a solution of triphenylphosphane (9.18 g, 35.0 mmol) in dichloromethane (80 mL). After stirring at –20 °C for 30 min, 2-(11′-dodecen-5′-ynyloxy)-tetrahydro-2*H*-pyran (**27**) (4.0 g, 15.1 mmol) was added to the colorless suspension of the triphenylphosphane–bromine complex, and stirring was continued at ambient temperature for 20 h. After work-up, the residue was purified by column chromatography (80 g of silica gel, column 2.5 × 40 cm, pentane) to furnish 1.84 g (50%) of **29** as a colorless liquid. R_f (pentane) = 0.51. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.47 [m, 4 H, 4(5)-H], 1.64 (tt, ^3J = 7, ^3J = 7 Hz, 2 H, 10-H), 1.96 (tt, ^3J = 7, ^3J = 7 Hz, 2 H, 11-H), 2.04 (m, 2 H, 3-H), 2.16 [m, 4 H, 6(9)-H], 3.43 (t, ^3J = 6.8 Hz, 2 H, 12-H), 4.94 (d, ^3J = 10 Hz, 1 H, 1-H), 4.99 (d, ^3J = 17 Hz, 1 H, 1-H), 5.80 (m_c, 1 H, 2-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 17.88 (C-9), 18.52 (C-6), 27.39 (C-10*), 27.99 (C-5*), 28.43 (C-4*), 31.68 (C-11**), 33.22 (C-3**), 33.37 (C-12**), 79.22 (C-7), 80.73 (C-8), 114.45 (C-1), 138.67 (C-2) ppm. MS (DCI, NH_3): *m*/*z* (%) = 262/260 (100:90) [M + NH_4^+].

Diethyl 2-(9′-Decen-3′-ynyl)malonate (31): Following GP2, diethyl malonate (3.68 g, 23.0 mmol) was added dropwise at room temperature to a mixture of sodium hydride (1.0 g, 25.0 mmol, 60% oil suspension) and anhydrous DMSO (50 mL). The resulting clear solution was transferred into a solution of 10-bromo-1-decen-7-yne (**28**) (3.32 g, 15.4 mmol) in DMSO (5.0 mL), and stirring was continued for 30 h. After work-up, the residue was purified by column chromatography (120 g of silica gel, column 5 × 25 cm, PE/Et_2O, 20:1) to afford 2.89 g (64%) of diethyl 2-(9′-decen-3-ynyl)-malonate (**31**) as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.28. IR (film): $\tilde{\nu}$ = 3076 (CH), 2979, 2934, 2858, 1734 (C=O), 1641 (C=C), 1446, 1370, 1249, 1156, 1097, 1049, 915, 862 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.26 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.48 [m, 4 H, 6′(7′)-H], 2.06 [m, 4 H, 1′(8′)-H], 2.16 (m, 2 H, 2′-H), 2.23 (m, 2 H, 5′-H), 3.41 (t, ^3J = 7.4 Hz, 1 H, 2-H), 4.19 (q, ^3J = 7.1 Hz, 4 H, OCH_2), 4.94 (d, ^3J = 10.1 Hz, 1 H, 10′-H), 5.00 (d, ^3J = 17.1 Hz, 1 H, 10′-H), 5.79 (m, 1 H, 9′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.01 (2 OCH_2CH_3), 16.69 (C-2′), 18.49 (C-5′), 27.94 (C-6′, C-7′), 28.32 (C-1′), 33.21 (C-8′), 50.61 (C-2), 61.34 (2 OCH_2), 78.01 (C-3′*), 81.52 (C-4′*), 114.44 (C-10′), 138.63 (C-9′), 169.18 (2 C=O) ppm. MS (DCI, NH_3): *m*/*z* (%) = 606 (25) [2M + NH_4^+], 312 (100) [M + NH_4^+].

Diethyl 2-(10′-Undecen-4′-ynyl)malonate (32): Following GP2, diethyl malonate (1.81 g, 11.3 mmol) was added dropwise at room temperature to a mixture of sodium hydride (0.48 g, 12 mmol, 60% oil suspension) and anhydrous DMF (15 mL). The clear solution was transferred into a solution of 11-bromo-1-undecen-7-yne (**29**) (2.03 g, 8.9 mmol) in DMF (5.0 mL), and stirring was continued for 1 d. After work-up, the resulting residue was purified by column chromatography (40 g of silica gel, column 2 × 30 cm, PE/Et_2O, 20:1) to afford 1.62 g (60%) of **32** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.29. IR (film): $\tilde{\nu}$ = 3076 , 2933, 2860, 1734 (C=O), 1641 (C=C), 1446, 1369, 1151, 1097, 1031, 865 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.25 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.46 [m, 6 H, 2′(7′, 8′)-H], 2.0 [m, 4 H, 1′(9′)-H], 2.15 [m, 4 H, 3′(6′)-H], 3.33 (t, ^3J = 7.6 Hz, 1 H, 2-H), 4.17 (q, ^3J = 7.1 Hz, 4 H, OCH_2), 4.93 (d, ^3J = 10 Hz, 1 H, 11′-H), 4.98 (d, ^3J = 17 Hz, 1 H, 11′-H), 5.78 (m_c, 1 H, 10′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.03 (2 OCH_2CH_3), 18.42 (C-3′*), 18.51 (C-6′*), 26.69 (CH_2), 27.83 (CH_2), 27.98 (CH_2), 28.41 (CH_2), 33.22 (C-9′), 51.56 (C-2),

61.28 (2 OCH_2), 79.08 (C-4′*), 80.68 (C-5′*), 114.41 (C-11′), 138.68 (C-10′), 169.32 (2 C=O) ppm. MS(70 eV, EI): *m/z* (%) = 308 (0.3) [M^+], 189 (55), 173 (46), 161 (62), 160 (100) [$M^+ - (C_6H_{10}O_4 + 2\ H)$], 148 (73), 133 (65), 119 (76), 93 (64), 91 (83), 80 (60), 79 (89), 67 (50), 55 (37), 41 (56).

Diethyl 2-(11′-Dodecen-5′-ynyl)malonate (33): Following GP2, diethyl malonate (1.36 g, 8.5 mmol) was added dropwise at room temperature to a mixture of sodium hydride (0.34 g, 8.5 mmol, 60% oil suspension) and anhydrous DMF (10 mL). The resulting clear solution was transferred into a solution of 12-bromo-1-dodecen-7-yne (**30**) (1.84 g, 7.6 mmol) in DMF (5.0 mL), and stirring was continued for 1 d. After work-up, the residue was purified by column chromatography (40 g of silica gel, column 2 × 30 cm, PE/Et_2O, 20:1) to afford 1.87 g (77%) of **33** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.26. IR (film): ṽ = 2980 , 2931 (CH), 1733 (C=O), 1641 (C=C), 1457, 1369, 1194, 1110, 1030, 853 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.0 Hz, 6 H, OCH_2CH_3), 1.45 [m, 8 H, 2′(3′, 8′, 9′)-H], 1.87 (dt, ^3J = 7.6, ^3J = 7.6 Hz, 2 H, 1′-H), 1.99–2.15 [m, 6 H, 4′(7′, 10′)-H], 3.29 (t, ^3J = 7.6 Hz, 1 H, 2-H), 4.16 (q, ^3J = 7.0 Hz, 4 H, OCH_2), 4.92 (d, ^3J = 10 Hz, 1 H, 12′-H), 4.98 (d, ^3J = 17 Hz, 1 H, 12′-H), 5.83 (m_c, 1 H, 11′-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.01 (2 OCH_2CH_3), 18.44 (C-4′*), 18.50 (C-7′*), 26.45 (C-2′), 27.97 (CH_2), 28.23 (CH_2), 28.44 (CH_2), 28.63 (CH_2), 33.20 (C-10′), 51.88 (C-2), 61.22 (2 OCH_2), 79.65 (C-5′**), 80.24 (C-6′**), 114.39 (C-12′), 138.65 (C-11′), 169.40 (2 C=O) ppm. MS (DCI, NH_3): *m/z* (%) = 662 (10) [2M + NH4$^+$], 340 (100) [M + NH_4^+].

Diethyl 2-Bromotetradeca-1,13-diene-7-yne-4,4-dicarboxylate (34): Following GP2, diethyl 2-(9′-decen-3′-ynyl)malonate (**31**) (2.89 g, 9.82 mmol) was added dropwise at room temperature to a mixture of sodium hydride (0.47 g, 11.7 mmol, 60% oil suspension) and DME (20 mL). After stirring for 30 min, 2,3-dibromopropene (3.0 g, 15.0 mmol) was added, and stirring was continued for 5 h. After work-up, the residue was purified by column chromatography (80 g of flash silica gel, column 2.5 × 40 cm, PE/Et_2O, 30:1) to afford 3.35 g (83%) of **34** as a colorless oil. R_f (PE/Et_2O, 20:1) = 0.26. IR (film): ṽ = 2975 (CH), 2934, 2859, 1733 (C=O), 1625 (C=C), 1446, 1368, 1262, 1186, 1097, 1024, 908, 861, 803 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.25 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.45 [m, 4 H, 10(11)-H], 2.11 [m, 6 H, 5(6,12)-H], 2.20 (m, 2 H, 9-H), 3.15 (s, 2 H, 3-H), 4.18 (q, ^3J = 7.1 Hz, 4 H, OCH_2), 4.93 (d, ^3J = 10.0 Hz, 1 H, 14-H), 4.99 (d, ^3J = 17.2 Hz, 1 H, 14-H), 5.58 (d, ^2J = 1.6 Hz, 1 H, 1-H), 5.67 (d, ^2J = 1.7 Hz, 1 H, 1-H), 5.78 (m_c, 1 H, 13-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.92 (2 OCH_2CH_3), 14.20 (C-6), 18.57 (C-9), 28.00 (C-10*), 28.31 (C-11*), 31.01 (C-5), 33.22 (C-12), 42.94 (C-3), 56.43 (C-4), 61.61 (2 OCH_2), 78.49 (C-7**), 80.70 (C-8**), 114.45 (C-14), 121.86 (C-1), 127.06 (C-2), 138.65 (C-13), 170.10 (2 C=O) ppm. MS (DCI, NH_3): *m/z* (%) = 846/844/842 (9:18:7) [2M + NH_4^+], 433/432/431/430 (18:100:18:96) [M + NH_4^+]. $C_{20}H_{29}BrO_4$ (413.4): calcd. C 58.11, H 7.07; found C 58.06, H 7.22.

Diethyl 2-Bromopentadeca-1,14-dien-8-yne-4,4-dicarboxylate (35): Following GP2, diethyl 2-(10′-undecen-4′-ynyl)malonate (**32**) (1.62 g, 5.25 mmol) was added dropwise at room temperature to a mixture of sodium hydride (0.22 g, 5.5 mmol, 60% oil suspension) and DME (10 mL). After stirring for 30 min, 2,3-dibromopropene (1.2 g, 6.0 mmol) was added, and stirring was continued for 12 h. After work-up, the residue was purified by column chromatography (40 g of flash silica gel, column 2.0 × 30 cm, PE/Et_2O, 25:1) to afford 1.71 g (76%) of **34** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.32. IR (film): ṽ = 3075 , 2978, 2934, 2860, 1733 (C=O), 1626 (C=C), 1445, 1367, 1277, 1180, 1095, 1038, 910, 859 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.46 [m, 6 H, 6(11,12)-H], 2.03–2.18 [m, 8 H, 5(7,10,13)-H], 3.14 (s, 2 H, 3-H), 4.19 (q, ^3J = 7.1 Hz, 4 H, OCH_2), 4.92 (d, ^3J = 10.1 Hz, 1 H, 15-H), 4.98 (d, ^3J = 16.9 Hz, 1 H, 15-H), 5.55 (d, ^2J = 2 Hz, 1 H, 1-H), 5.65 (d, ^2J = 2 Hz, 1 H, 1-H), 5.79 (m_c, 1 H, 14-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.95 (2 OCH_2CH_3), 18.53 (C-7*), 18.89 (C-10*), 23.87 (C-6), 28.01 (C-11**), 28.43 (C-12**), 30.60 (C-5), 33.24 (C-13), 42.74 (C-3), 56.71 (C-4), 61.50 (2 OCH_2), 79.17 (C-8***), 80.58 (C-9***), 114.44 (C-15), 121.63 (C-1), 127.23 (C-2), 138.67 (C-14), 170.44 (2 C=O) ppm. MS (DCI, NH_3): *m/z* (%) = 447/446/445/444 (22:100:21:92) [M + NH_4^+]. $C_{21}H_{31}BrO_4$ (427.4): calcd. C 59.02, H 7.31; found C 59.17, H 7.34.

Diethyl 2-Bromohexadeca-1,15-dien-9-yne-4,4-dicarboxylate (36): Following GP2, diethyl 2-(11′-dodecen-5′-ynyl)malonate (**33**) (1.87 g, 5.8 mmol) was added dropwise at room temperature to a mixture of sodium hydride (0.24 g, 6.0 mmol, 60% oil suspension) and DME (12 mL). After stirring for 30 min, 2,3-dibromopropene (1.4 g, 7.0 mmol) was added, and stirring was continued for 12 h. After work-up, the residue was purified by column chromatography (40 g of flash silica gel, column 2.0 × 30 cm, PE/Et_2O, 20:1) to afford 1.70 g (66%) of **36** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.30. IR (film): ṽ = 2933 (CH), 2859, 1735 (C=O), 1626 (C=C), 1463, 1282, 1237, 1175, 1097, 1036, 911, 859 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.45 [m, 8 H, 6(7,12,13)-H], 1.94–2.15 [m, 8 H, 5(8,11,14)-H], 3.16 (s, 2 H, 3-H), 4.17 (q, ^3J = 7.1 Hz, 4 H, OCH_2), 4.93 (d, ^3J = 11 Hz, 1 H, 16-H), 4.98 (d, ^3J = 17 Hz, 1 H, 16-H), 5.55 (d, ^2J = 2 Hz, 1 H, 1-H), 5.64 (d, ^2J = 2 Hz, 1 H, 1-H), 5.78 (m_c, 1 H, 15-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.95 (2 OCH_2CH_3), 18.42 (C-8*), 18.53 (C-11*), 22.99 (C-6), 28.02 (C-7**), 28.49 (C-12**), 29.09 (C-13**), 30.63 (C-5), 33.23 (C-14), 42.60 (C-3), 56.87 (C-4), 61.45 (2 OCH_2), 79.69 (C-9***), 80.23 (C-10***), 114.45 (C-16), 121.55 (C-1), 127.38 (C-2), 138.64 (C-15), 170.54 (2 C=O) ppm. MS (DCI, NH_3): *m/z* (%) = 903/902/901/900/899/898 (23:50:38:80:22:40) [2M + NH_4^+], 461/460/459/458 (22:100:22:99) [M + NH_4^+]. $C_{22}H_{33}BrO_4$ (441.4): calcd. C 59.86, H 7.54; found C 59.58, H 7.96.

General Procedure for Palladium-Catalyzed Oligocyclizations of 2-Bromoalka-1,(*n*+*m*+1)-dien-(*n*+1)-ynes Initiated by a Heck-Type Reaction (GP5)

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 or silver carbonate (2.5 equiv.), and the respective 2-bromoalka-1,(*n*+*m*+1)-dien-(*n*+1)-yne (1 equiv.) in acetonitrile. After stirring at 60 °C for 1 to 12 h, the reaction mixture is allowed to cool to room temperature, filtered through a layer each of Celite® and of charcoal, then concentrated. The residue is purified by column chromatography.

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.) or silver carbonate (3.0 equiv.), and of the respective precursor 2-bromoalka-1,(*n*+*m*+1)-dien-(*n*+1)-yne (1 equiv.) in DMF. After stirring at 80 °C from 1 to 12 h, the reaction mixture is poured into water (30 mL) and the mixture extracted with diethyl ether (3 × 20 mL). The combined ether layers are dried ($MgSO_4$), concentrated, and the residue is purified by column chromatography.

Palladium-Catalyzed Oligocyclization of Dimethyl 2-Bromotrideca-1,12-diene-7-yne-4,4-dicarboxylate (8): Following GP5, method A, dimethyl 2-bromotrideca-1,12-diene-7-yne-4,4-dicarboxylate (**8**) (371 mg, 1.0 mmol) upon treatment at 80 °C with palladium acetate (22 mg, 0.10 mmol), triphenylphosphane (66 mg, 0.25 mmol) and

silver carbonate (828 mg, 3.0 mmol) in acetonitrile (10 mL), after 16 h, work-up and purification by column chromatography (20 g of flash silica gel, column 1 × 35 cm, PE/Et_2O, 20:1), afforded the following fractions:

Fraction I: 88 mg (30%) of dimethyl tricyclo[7.4.0.0^{2,6}]trideca-1(9),2(6)-diene-11,11-dicarboxylate (**37**) as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.25. IR (film): $\tilde{\nu}$ = 3436 , 2978, 2869, 2086, 1635 (C=O), 1383, 1350, 1124, 1077, 640 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.84 (tt, ^3J = 7, ^3J = 7 Hz, 2 H, 4-H), 2.14 [m, 8 H, 7(8,12,13)-H], 2.30 [t, ^3J = 7 Hz, 4 H, 3(5)-H], 2.55 (br. s, 2 H, 10-H), 3.70 (s, 6 H, OCH_3) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 22.41 (C-4), 22.94 (C-13), 23.88 (C-8*), 27.84 (C-12), 29.16 (C-7*), 30.97 (C-3), 34.97 (C-10), 35.50 (C-5), 52.56 (OCH_3), 52.63 (OCH_3), 53.33 (C-4), 124.20, 124.91, 134.04, 134.33, 172.02 (2 C=O) ppm. MS (70 eV, EI): *m*/*z* (%) = 290 (9) [M$^+$], 288 (8) [M$^+$ – 2 H], 230 (50), 229 (36), 228 (96), 169 (100), 141 (62), 129 (28), 115 (21), 59 (31).

Fraction II: 52 mg (18%) of dimethyl tricyclo[7.4.0.0^{2,6}]trideca-1(9),2(6),7-triene-11,11-dicarboxylate (**38**) as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.21. IR (film): $\tilde{\nu}$ = 2951 , 2841, 1736 (C=O), 1484, 1436, 1258, 1087, 1068, 1025, 807 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ = 1.77 (tt, ^3J = 7.4, ^3J = 7.4 Hz, 2 H, 4-H), 2.41 (t, ^3J = 7 Hz, 2 H, 12-H), 2.46 (t, ^3J = 7 Hz, 2 H, 5-H), 2.63 (t, ^3J = 6.8 Hz, 2 H, 13-H), 2.69 (t, ^3J = 7.4 Hz, 2 H, 3-H), 3.27 (s, 6 H, OCH_3), 3.43 (br. s, 2 H, 10-H), 6.91 (d, ^3J = 7.7 Hz, 1 H, 7-H), 6.96 (d, ^3J = 7.7 Hz, 1 H, 8-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 23.73 (–, C-13), 24.74 (-, C-4), 28.02 (–, C-12), 30.88 (–, C-5), 32.66 (–, C-3), 34.61 (C-10), 52.65 (+, 2 OCH_3), 53.46 (C_{quat}, C-11), 121.90 (+, C-8), 126.83 (+, C-7), 130.24 (C_{quat}), 130.55 (C_{quat}), 141.67 (C_{quat}), 142.45 (C_{quat}), 171 (C_{quat}, 2 C=O) ppm. MS (70 eV, EI): *m*/*z* (%) = 288 (29) [M$^+$], 228 (100), 169 (87), 141 (30). HRMS: calcd. for $C_{17}H_{20}O_4$ (288.3): 288.1361 (correct mass).

Diethyl 13-Methoxytricyclo[7.4.0.0^{2,6}]trideca-1(9),2(6)-diene-4,4-dicarboxylate (39): Following GP5, method A, diethyl 2-bromo-8-methoxytrideca-1,12-dien-6-yne-4,4-dicarboxylate (**11**) (300 mg, 0.7 mmol) upon treatment at 80 °C with palladium acetate (8.0 mg, 0.036 mmol), triphenylphosphane (19 mg, 0.072 mmol) and silver carbonate (580 mg, 2.10 mmol) in acetonitrile (10 mL), after 16 h, work-up and purification by column chromatography (20 g of flash silica gel, column 1.5 × 20 cm, PE/Et_2O, 10:1), afforded, in addition to a complex mixture of inseparable products, 90 mg (37%) of **39** as a colorless oil. IR (film): $\tilde{\nu}$ = 2930 , 1733 (C=O), 1446, 1258, 1185, 1096 (C–O), 862, 800 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 (m, 6 H, OCH_2CH_3), 1.4–1.9 [m, 6 H, 10(11,12)-H], 2.07–2.13 [m, 4 H, 7(8)-H], 2.9–3.2 [m, 4 H, 3(5)-H], 3.38 (s, 3 H, OCH_3), 3.45 (m, 1 H, 13-H), 4.18 (m, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.03 (+, 2 OCH_2CH_3), 17.54 (–, C-11), 23.05 (–, CH_2), 25.89 (–, C-12), 29.50 (–, CH_2), 30.30 (–, CH_2), 39.56 (–, C-3), 43.26 (–, C-5), 55.85 (+, OCH_3), 58.74 (C_{quat}, C-4), 61.35 (–, OCH_2), 61.42 (–, OCH_2), 73.51 (+, C-13), 125.87 (C_{quat},C-9), 130.72 (C_{quat}, C-6), 131.30 (C_{quat}, C-1), 134.28 (C_{quat}, C-2), 172.09 (C_{quat}, C=O), 172.69 (C_{quat}, C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 348 (41) [M$^+$], 316 (61) [M$^+$ – CH_3OH], 275 (19), 242 (100), 197 (12), 169 (61), 143 (20), 91 (15), 57 (13), 44 (19).

Diethyl 4,4-Dimethy-3-oxotricyclo[7.5.0.0^{2,6}]tetradeca-1(9),2(6)-diene-11,11-dicarboxylate (40): Following GP5, method A, diethyl 2-bromo-11,11-dimethyl-10-oxotetradeca-1,13-dien-8-yne-4,4-dicarboxylate (**17**) (455 mg, 1.0 mmol) upon treatment at 80 °C with palladium acetate (22.0 mg, 0.10 mmol), triphenylphosphane (66 mg, 0.25 mmol) and silver carbonate (828 mg, 3.0 mmol) in acetonitrile (10 mL), after 4 d, work-up and purification by column chromatography (20 g of flash silica gel, column 1.0 × 35 cm, PE/Et_2O, 5:1), afforded 124 mg (33%) of **40** as a colorless oil. R_f (PE/Et_2O, 5:1) = 0.17. IR (film): $\tilde{\nu}$ = 2958 (CH), 2864, 1732 (C=O), 1695 (C=O), 1639 (C=C), 1603, 1447, 1390, 1316, 1261, 1225, 1095 cm^{-1}. 1035, 861, 799. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.03 (s, 6 H, 4-CH_3), 1.20 (m, 2 H, 13-H), 1.21 (t, ^3J = 7.1 Hz, 6 H, OCH_2CH_3), 1.59 (m, 2 H, 12-H), 2.15 (m_c, 2 H, 14-H), 2.34 [m, 5 H, 5(7, 8)-H], 2.76 [m, 3 H, 5(10)-H], 4.10 (m, 4 H, OCH_2) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.94 (+, 2 OCH_2CH_3), 22.29 (–, C-13), 25.27 (+, 2 4-CH_3), 25.52 (–, C-8*), 26.80 (–, C-7*), 30.68 (–, C-12), 36.96 (–, C-14), 38.68 (–, C-10), 44.25 (C_{quat}, C-4), 45.37 (–, C-5), 55.21 (C_{quat}, C-11), 61.05 (–, 2 OCH_2), 131.84 (C_{quat}), 132.08 (C_{quat}), 133.81 (C_{quat}), 169.74 (C_{quat}, C-6), 171.56 (C_{quat}, 2 C=O), 210.22 (C_{quat}, C-14) ppm. MS (DCI, NH_3): *m*/*z* (%) = 766 (12) [2M + NH_4^+], 392 (100) [M + NH_4^+].

Palladium-Catalyzed Oligocyclization of 10-(2′-Bromoallyloxy)-4,4-dimethyl-5-methoxy-1-decen-6-yne (20): Following GP5, method B, 10-(2′-bromoallyloxy)-4,4-dimethyl-5-methoxy-1-decen-6-yne (**20**) (329 mg, 1.0 mmol) upon treatment at 80 °C with palladium acetate (22 mg, 0.10 mmol), triphenylphosphane (66 mg, 0.25 mmol) and silver carbonate (828 mg, 3.0 mmol) in DMF (10 mL), after 5 d, work-up and purification by column chromatography (20 g of flash silica gel, column 1 × 35 cm, PE/Et_2O, 5:1), afforded 69 mg (48%) of a 9:1 mixture of **41** and **42**. Further two purifications by column chromatography (20 g of flash silica gel, column 1 × 35 cm, PE/Et_2O, 5:1) afforded 25 mg (17%) of pure 10-methoxy-9,9-dimethyl-2,3,5,6,7,8,9,10-octahydro-1*H*-indeno[5,4-*c*]oxepine (**41**) as a colorless oil. R_f (PE/Et_2O, 5:1) = 0.13. IR (film): $\tilde{\nu}$ = 2932 (CH), 1721 (C=O), 1465, 1384, 1364, 1263, 1098, 1030, 736, 703 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.06 (s, 3 H, 9-CH_3), 1.12 (s, 3 H, 9-CH_3), 1.84 (m, 2 H, 2-H), 1.95 (d, ^2J = 17.1 Hz, 1 H, 8-H), 2.08 [m, 4 H, 6*(7*)-H], 2.36 (d, ^2J = 17.1 Hz, 1 H, 8-H), 2.47 (m, 2 H, 1-H*), 3.34 (s, 3 H, OCH_3), 3.79 (s, 1 H, 10-H), 3.82 (ddd, ^2J = 6, ^3J = 6, ^3J = 3 Hz, 2 H, 3-H), 4.13 (br. s, 2 H, 5-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 22.91 (+,9-CH_3), 24.13 (–, C-6*), 26.54 (–, C-7*), 27.67 (–, C-2**), 28.61 (–, C-1**), 30.13 (+,9-CH_3), 41.58 (C_{quat}, C-9), 49.58 (–, C-8), 57.58 (+, OCH_3), 71.86 (–, C-3***), 72.47 (–, C-5***), 92.53 (+, C-10), 131.06 (C_{quat}), 131.61 (C_{quat}), 135.09 (C_{quat}), 138.89 (C_{quat}) ppm. MS (70 eV, EI): *m*/*z* (%) = 249 (17) [M$^+$ + H], 248 (100) [M$^+$], 216 (39), 201 (25), 173 (32), 162 (34), 159 (31), 145 (22). HRMS: calcd. for $C_{16}H_{24}O_2$ (248.4): 248.1776 (correct mass).

A mixture (44.0 mg) of **41** and **42** was added at ambient temperature into a dark-red solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (46 mg, 0.20 mmol) in benzene (20 mL). After stirring for 30 min, Et_2O (20 mL) and sodium hydroxide solution (1%, 10 mL) were added. The two layers were separated, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the resulting residue was purified by column chromatography (10 g of flash silica gel, column 1 × 15 cm, PE/Et_2O, 5:1) to afford 40 mg (92%) of pure 10-methoxy-9,9-dimethyl-2,3,5,8,9,10-hexahydro-1*H*-indeno[5,4-*c*]oxepine (**42**) as a colorless oil. R_f (PE/Et_2O, 5:1) = 0.17. IR (film): $\tilde{\nu}$ = 3073 (CH), 2974, 2871, 1732 (C=O), 1626 (C=C), 1446, 1367, 1278, 1181, 1029, 914 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.00 (s, 3 H, 9-CH_3), 1.26 (s, 3 H, 9-CH_3), 1.83 (m, 2 H, 2-H), 2.49 (d, ^2J = 15.6 Hz, 1 H, 8-H), 2.94 (d, ^2J = 15.6 Hz, 1 H, 8-H), 3.06 (m, 2 H, 1-H), 3.39 (s, 3 H, OCH_3), 4.05 (m_c, 2 H, 3-H), 4.26 (s, 1 H, 10-H), 4.65 (s, 2 H, 5-H), 6.95 (d, ^3J = 7.5 Hz, 1 H, 6-H*), 7.06 (d, ^3J = 7.5 Hz, 1 H, 7-H*) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 22.58 (+,9-CH_3), 28.46 (+, 9-CH_3), 30.10 (–, C-2), 30.45 (–, C-1), 43.34 (C_{quat}, C-9), 45.85 (–, C-8), 57.50 (+, OCH_3), 74.76 (–, C-5), 75.45 (–, C-3), 90.43 (+, C-10), 122.46 (+, C-6), 129.25 (+, C-7), 138.40 (C_{quat}), 140.73 (C_{quat}),

140.84 (C_{quat}), 143.72 (C_{quat}) ppm. MS (DCI, NH_3): *m/z* (%) = 281 (19) [(M + NH_3) + NH_4^+], 264 (52) [M + NH_4^+], 249 (92) [(M – CH_3) + NH_4^+], 232 (100) [(M – OCH_3) + NH_4^+]. $C_{16}H_{22}O_2$ (246.4): calcd. C 78.01, H 9.00; found C 77.79, H 9.00.

Diethyl Tetracyclo[7,4,1,0^{1,9},0^{2,7}]tetradec-2-ene-11,11-dicarboxylate (43): Following GP5, method A, diethyl 2-bromotetradeca-1,13-diene-7-yne-4,4-dicarboxylate (**34**) (207 mg, 0.50 mmol) upon treatment at 80 °C with palladium acetate (11.0 mg, 0.05 mmol), triphenylphosphane (33 mg, 0.13 mmol) and silver carbonate (414 mg, 1.50 mmol) in acetonitrile (5 mL), after 3 d, work-up and purification by filtering over a layer each of Celite®, flash silica gel and charcoal, afforded 124 mg (74%) of **43** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.25. IR (film): $\tilde{\nu}$ = 2923 (CH), 2855, 1733 (C=O), 1448, 1251, 1202, 1173, 1087, 1077, 1041, 863 cm^{-1}. ^1H NMR (300 MHz, C_6D_6): δ = 0.38 (d, ^2J = 4.6 Hz, 1 H, 14-H), 0.80 (d, ^2J = 4.6 Hz, 1 H, 14-H), 0.90 (m, 6 H, OCH_2CH_3), 1.1 (m, 1 H, 6-H*), 1.35 (m, 1 H, 5-H*), 1.63 (m, 1 H, 5-H*), 1.65–1.85 [m, 5 H, 4(6,7,8,12)-H], 1.86 (d, ^2J = 14.2 Hz, 1 H, 10-H), 1.91–2.03 [m, 4 H, 4*(8,13)-H], 2.35 (m, 1 H, 12-H*), 2.85 (dd, ^2J = 14.2, ^4J = 1.6 Hz, 1 H, 10-H), 3.90 (m, 4 H, OCH_2), 5.28 (m, 1 H, 3-H) ppm. ^{13}C NMR (62.9 MHz, C_6D_6, DEPT): δ = 13.98 (+, OCH_2CH_3), 14.19 (+,OCH_2CH_3), 21.33 (–, C-4), 21.46 (–, C-14), 23.12 (–, C-5*), 25.06 (–, C-13*), 26.23 (–, C-12*), 28.03 (C_{quat}, C-9), 29.15 (–, C-6*), 30.51 (C_{quat}, C-1), 35.56 (+, C-7), 35.80 (–, C-10), 41.22 (–, C-8), 53.90 (C_{quat}, C-11), 61.01 (–, 2 OCH_2), 113.40 (+, C-3), 148.99 (C_{quat}, C-2), 170.96 (C_{quat}, C=O), 172.31 (C_{quat}, C=O) ppm. MS (70 eV, EI): *m/z* (%) = 332 (72) [M^+], 258 (100) [M^+ – $C_4H_{10}O$], 185 (63), 173 (28), 145 (21). HRMS: calcd. for $C_{20}H_{28}O_4$ (332.4): 332.1987 (correct mass).

Diethyl Tetracyclo[7,5,1,0^{1,9},0^{2,7}]pentadec-2-ene-11,11-dicarboxylate (44): Following GP5, method A, diethyl 2-bromopentadeca-1,14-dien-8-yne-4,4-dicarboxylate (**35**) (214 mg, 0.50 mmol) upon treatment at 70 °C with palladium acetate (11.0 mg, 0.05 mmol), triphenylphosphane (33 mg, 0.13 mmol) and silver carbonate (414 mg, 1.50 mmol) in acetonitrile (5 mL), after 3 d, work-up and purification by filtration through a layer each of Celite®, flash silica gel and charcoal, afforded 132 mg (76%) of **44** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.32. IR (film): $\tilde{\nu}$ = 2979 , 2869, 1731 (C=O), 1642 (C=O), 1382, 1130, 801, 658, 494 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.45 (d, ^2J = 4.7 Hz, 1 H, 15-H), 0.84 (d, ^2J = 4.7 Hz, 1 H, 15-H), 1.21 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.23 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.20–1.55 (m, 2 H), 1.68–1.96 (m, 11 H), 2.00 (m, 2 H), 2.13 (d, ^2J = 15.6 Hz, 1 H, 10-H), 2.19 (m, 2 H), 2.61 (d, ^2J = 15.6 Hz, 1 H, 10-H), 4.13 (m, 4 H, OCH_2), 5.26 (br. s, 1 H, 3-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.91 (+, OCH_2CH_3), 14.00 (+, OCH_2CH_3), 21.45 (–, CH_2), 22.72 (–, CH_2), 24.65 (–, 2 CH_2), 27.62 (–, CH_2), 29.14 (–, CH_2), 30.77 (C_{quat}, C-9), 33.02 (–, CH_2), 34.69 (C_{quat}, C-1), 35.06 (+, C-7), 37.13 (–, C-10*), 38.43 (–, C-8*), 57.08 (C_{quat}, C-11), 60.97 (–, OCH_2), 61.15 (–, OCH_2), 113.91 (+, C-3), 146.46 (C_{quat}, C-2), 172.16 (C_{quat}, C=O), 172.75 (C_{quat}, C=O) ppm. MS (DCI, NH_3): *m/z* (%) = 710 (12) [2M + NH_4^+], 364 (16) [M + NH_4^+], 347 (100). $C_{21}H_{30}O_4$ (346.5): calcd. C 72.80, H 8.73; found C 72.84, H 8.70.

Diethyl Tetracyclo[7,6,1,0^{1,9},0^{2,7}]hexadec-2-ene-11,11-dicarboxylate (45): Following GP5, method A, diethyl 2-bromohexadeca-1,15-dien-9-yne-4,4-dicarboxylate (**36**) (207 mg, 0.47 mmol) upon treatment at 80 °C with palladium acetate (11.0 mg, 0.05 mmol), triphenylphosphane (33 mg, 0.13 mmol) and silver carbonate (414 mg, 1.50 mmol) in acetonitrile (5 mL), after 3 d, work-up and purification by filtering over a layer each of Celite®, flash silica gel and charcoal, afforded 51 mg (30%) of **45** as a colorless oil. R_f (PE/Et_2O, 10:1) = 0.25. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.22 (d, ^2J = 3.8 Hz, 1 H, 16-H), 0.80 (d, ^2J = 3.8 Hz, 1 H, 16-H), 1.20 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 1.10–1.30 (m, 1 H), 1.25 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 1.41 (m, 2 H), 1.55–1.75 (m, 7 H), 1.80–1.95 (m, 2 H), 1.85 (d, ^2J = 14.5 Hz, 1 H, 10-H), 2.00–2.17 (m, 3 H), 2.24–2.55 (m, 2 H), 2.85 (dd, ^2J = 14.5, J = 1.2 Hz, 1 H, 10-H), 4.15 (m, 4 H, OCH_2), 5.25 (m, 1 H, 3-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.04 (+, 2 OCH_2CH_3), 22.74 (–, C-4*), 23.06 (–, C-16*), 24.43 (–, CH_2), 24.63 (–, CH_2), 24.90 (–, CH_2), 28.90 (–, CH_2), 30.25 (–, CH_2), 30.58 (–, CH_2), 31.52 (C_{quat}, C-9), 34.22 (–, C-10**), 34.32 (+, C-7), 35.33 (C_{quat}, C-1), 35.84 (–, C-8**), 56.85 (C_{quat}, C-11), 61.18 (–, OCH_2), 61.28 (–, OCH_2), 114.77 (+, C-3), 145.46 (C_{quat}, C-2), 171.74 (C_{quat}, C=O), 172.94 (C_{quat}, C=O) ppm. MS (70 eV, EI): *m/z* (%) = 362 (19) [M^+ + 2 H], 361 (20) [M^+ + H], 360 (100) [M^+], 347 (18), 315 (10), 286 (24), 240 (24), 213 (39), 200 (30), 173 (39), 160 (47), 159 (40), 145 (74), 131 (36), 105 (23), 91 (34).

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