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Stereoselective Syntheses of Dihydroxerulin and Xerulinic Acid, Anti-Hypocholesterolemic Dyes from the Fungus *Xerula melanotricha*

Achim Sorg,[a] Konrad Siegel,[b] and Reinhard Brückner*[a]

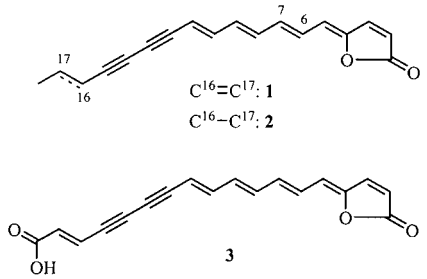
Abstract: The title compounds **2** and **3**, which are inhibitors of the biosynthesis of cholesterol, were synthesized in a convergent and perfectly stereoselective manner. In the key step, bromobutenolide **6** (obtained from levulinic acid in two steps) was coupled with either of the novel bis(stannanes) *trans,cis*-*trans*-**35** or *trans,trans,trans*-**35** [each accessible from 3-(tributylstannyl)allyl alcohol (**17**) in four steps], giving γ-alkylidenebutenolide *trans,trans,trans*-**32**. This compound was coupled with iododiyne **42** or the bromoenediynoate **44** leading to dihydroxerulin (**2**) and to the (trimethylsilylethyl)ester **45** of xerulinic acid, respectively. Deprotection of the latter provided totally synthetic xerulinic acid (**3**) for the first time.

Keywords: butenolides · C–C coupling · natural products · polyene · stannane

Introduction

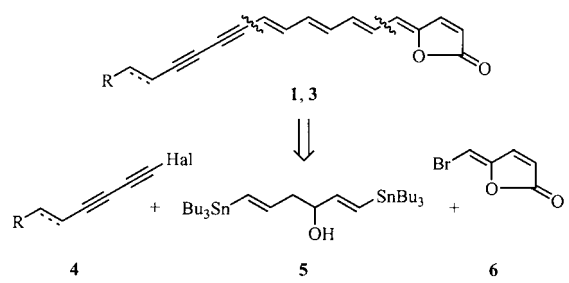
Some time ago, a collaboration of the groups of Anke and Steglich on constituents from the fungus *Xerula melanotricha* Dörfelt resulted in the isolation and structure elucidation of three heavily unsaturated, intensely yellow γ-alkylidenebutenolides:[1] xerulin (**1**), dihydroxerulin (**2**), and xerulinic acid (**3**; Scheme 1).[2] Xerulin and dihydroxerulin were characterized as 10:90–35:65 mixtures, whereas xerulinic acid was obtained pure. Each of these compounds suppressed the biosynthesis of cholesterol in human HeLa S3 cells through inhibition of HMG-SCoA synthase (EC 4.1.3.5).[2] In the same cell system, **3**—other than **1** and **2**—also suppressed the synthesis of RNA at $IC_{50} \approx 100$ μM.[2]

Even more than their pharmacologic activities, their structural uniqueness turned xerulin and its alikes into attractive synthetic targets. Siegel—from our group—achieved the first laboratory syntheses of dihydroxerulin (**2**)[3] and xerulin (**1**),[4] Rossi et al.[5] and Negishi/Alimardanov[6] the respective numbers two. The latest advent to these accomplishments has been our recently published total synthesis of xerulinic acid (**3**).[7,8] In the following, we disclose this synthesis in full detail. In addition, we describe the successful termination of a related route providing dihydroxerulin (**2**).



Scheme 1. Dyes from *Xerula melanotricha*.

Each of these syntheses utilized novel reagents. They were conceived starting from the unprecedented retrosynthetic disconnections shown in Scheme 2. They are distinct from our first approach to dihydroxerulin[3] and our approach to xerulin[4] since we would form C–C rather than



Scheme 2. Proposed retrosynthesis.

[a] Dr. A. Sorg, Prof. Dr. R. Brückner
Institut für Organische Chemie und Biochemie
Albert-Ludwigs-Universität
Albertstrasse 21, 79104 Freiburg (Germany)
Fax: (+49) 761-203-6100
E-mail: reinhard.brueckner@organik.chemie.uni-freiburg.de
[b] Dr. K. Siegel
Bayer Health Care AG, PH-OP-ELB-CE-VF
Building 64, 42096 Wuppertal (Germany)

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C=C bonds in the endgame. The latter approach—by Wittig reactions—was non-stereoselective[3,4] while the present approach was expected to be rigorously stereoselective: We wanted to establish the stereogenic C=C bonds correctly configured first and carry them on unaltered thereafter, that is, while joining appropriate precursors under Pd catalysis.[9] Because of the relative stability of organotin compounds under many reaction conditions, we were biased towards them, that is, aimed for Stille couplings[10] as key C–C bond forming steps. Based on this analysis, we chose terminally halogenated type-**4** enediynes, the conjunctive bis(stannane) **5**, and the previously unknown butenolide **6**[11] as the core intermediates of our approach. Ultimately, we replaced bis(stannane) **5** by either of its "dehydration products", that is, the novel hexatrienylbis(stannanes) *trans,cis,trans*- or *trans,trans,trans*-**35** (see Schemes 8 and 9, respectively). The transformations described in the following suggest that butenolide **6** may become as generally useful for making γ-alkylidenebutenolides as bis(stannanes) **35** in a general synthesis of conjugated trienes.

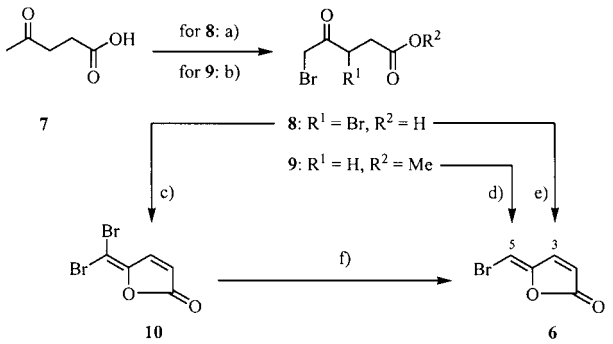
Results and Discussion

Initially, we derived the γ-(*mono*bromomethylene)butenolide **6** from the known γ-(*di*bromomethylene)butenolide **10** (Scheme 3). Compound **10** had been prepared more than a century ago[12] from the easily accessible dibromolevulinic acid **8**[13] but its structure was established much later.[14] The reagents providing **10** were 2:1 oleum/conc. H_2SO_4. Optimizing temperature and reaction times, we could prepare this compound without competing formation[12] of the isomeric α-bromo-γ-(bromomethylene)butenolide: The combination 50–60 °C/6 min provided **10** in 28% yield. (Monobromomethylene)butenolide **6** was formed by the *Z*-selective reduction of (dibromomethylene)butenolide **10** with stoich. Bu_3SnH/cat. $[Pd(PPh_3)_4]$ (method: see ref. [15]) which proceeded in 51% yield. All in all, this is a three-step synthesis of compound **6** from levulinic acid.[11]

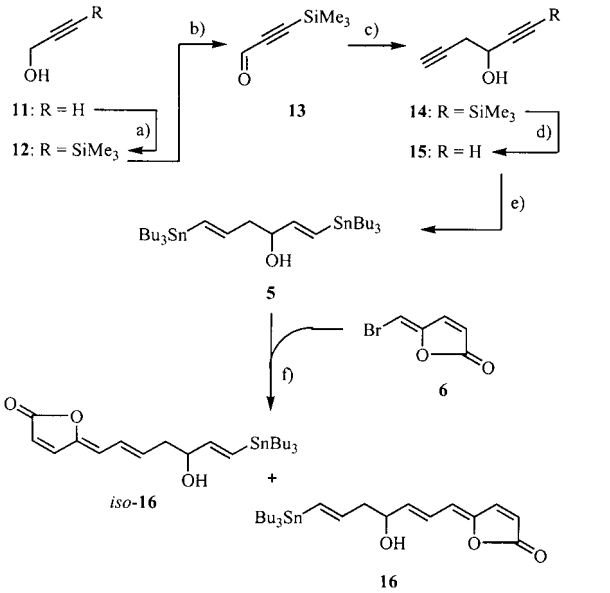
Alternatively, we treated methyl monobromolevulinate **9**[16] with concentrated H_2SO_4 at 100 °C for 20 min. Through lactonization of the tautomeric enol and oxidation, this rendered the same *Z*-configured (monobromomethylene)butenolide **6**. However, we could not increase its yield over 20%.

Subsequently, we short-cut this synthesis by treating dibromolevulinic acid **8** with a succession of two reagents (as indicated in the patent literature[17]): P_4O_{10} dehydrated—presumably by leading to an enolester containing a *Z*-configured BrHC=C–O group; addition of NEt_3[18] eliminated HBr. This two-step procedure was four times as high-yielding as the three-step access and as perfectly stereoselective.

The original center-piece **5** en route—according to the design of Scheme 2—to xerulinic acid was synthesized after C-silylating[19] propargyl alcohol (**11** → 72% **12**; Scheme 4).



Scheme 3. Synthesis of the butenolide fragment. a) Br_2 (2.1 equiv), CH_2Cl_2, 0 °C → RT, 2 h; 63% (ref.[13] 40%). b) Br_2 (1.0 equiv), MeOH, room temperature → Δ, 2 h; 38% (ref.[16] 30%). c) Ref.[11] oleum/conc. H_2SO_4 2:1 (*v*:*v*), 50–60 °C, 6 min; 28%. d) Conc. H_2SO_4, 100 °C, 20 min; 20%. e) i) P_4O_{10} (1.2 equiv), CH_2Cl_2, 0 °C → Δ, 1 h; filtration; ii) NEt_3 (1.03 equiv), CH_2Cl_2, 0 °C → Δ, 1 h; 55%. f) Ref.[11] Bu_3SnH (1.10 equiv), $[Pd(PPh_3)_4]$ (0.10 equiv), THF, 65 °C, 3 h; 51%. Positional numbers in compound **6** analogous to **1**–**3**.



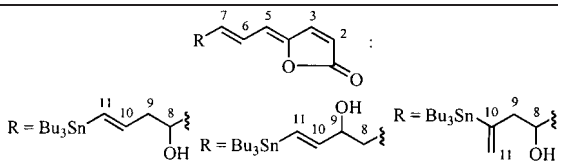
Scheme 4. a) BuLi (2.2 equiv), THF, −78 °C, 30 min, Me_3SiCl (2.2 equiv), → room temperature, 12 h; HCl (2 M), room temperature, 1 h; 72%. b) PCC on silica gel (*w*/*w* 1:1; 1.63 equiv), CH_2Cl_2, 0 °C, 8 h; 76%. c) Propargyl bromide (1.0 equiv), Mg (1.5 equiv), $HgCl_2$ (2 mol%), Et_2O, 0 °C, 90 min; **13**, −10 °C, 10 min, 0 °C, 1 h; used crude. d) K_2CO_3 (1.0 equiv), MeOH, RT, 14 h; 68% over the two steps. e) Bu_3SnH (3.0 equiv), AIBN (20 mol%), no solvent, 80 °C, 8 h; 60%. f) **5** (2.00 equiv), $[Pd(dba)_2]$ (4 mol%), $AsPh_3$ (15 mol%), addition of **6** in 20 min, THF, RT, 1 h; 55% (47:53 **16**:*iso*-**16**).

Oxidation with PCC[20] gave propiolaldehyde **13**[21] (76%). Addition of propargylmagnesium bromide (→**14**[22]) and desilylation with potassium carbonate in methanol[23] furnished hexadiynol **15**[24] (68% yield over the 2 steps). Radical-chain hydrostannylation[25] of both C≡C bonds was realized working *in* Bu_3SnH (3 equiv). It proceeded regio- and *trans*-selectively and yielded bis(stannane) **5** in 60% yield.

Bis(stannane) **5** caused an inconvenience when monocoupled with (bromomethylene)butenolide **6** (Scheme 4): The constitutional isomers **16** and *iso*-**16** arose as an inseparable 1:1 mixture. Hence, the two tributylstannyl groups in alcohol **5** differed with respect to their location but not their reactivity. This was not so much a nuisance synthetically: Each isomer—without the need for separation!—had to be treated identically in order to advance towards target **3**. Yet, the formation of a mixture of compounds **16**/*iso*-**16** and of isomeric mixtures derived therefrom were a nuisance spectroscopically: Structure identifications became tedious.

In order to identify the NMR resonances of monocoupling products **16** and *iso*-**16**, we synthesized compound **16** independently from the tin-containing alcohol **17** (Scheme 5); the latter was obtained from propargyl alcohol by cuprostannylation/protonolysis.[26] Dess–Martin oxidation[27] delivered the equally known[28] aldehyde **18**. 1,2-Addition of propargylmagnesium bromide rendered the tributylstannylated enynol **20**. Stille coupling[9] with the brominated butenolide **6** provided the C≡C-containing compound **21**. Its alkyne moiety was hydrostannylated with Bu_3SnH in the presence of 2 mol% of $[PdCl_2(PPh_3)_2]$—with stereo- but without regiocontrol. After flash chromatography on silica gel,[29] we isolated equal amounts of compounds **16** and **22**. The NMR spectra of the former allowed identifying the NMR signals of compound *iso*-**16** in the previously mentioned **16**/*iso*-**16** mixture (Scheme 4; Table 1).

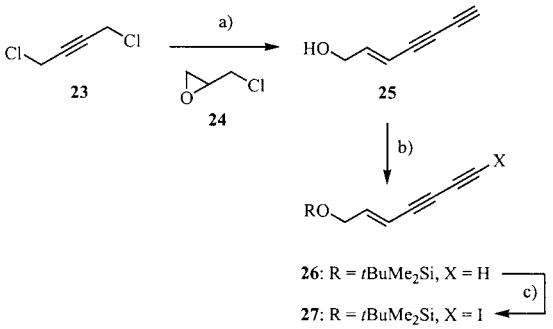
Table 1. ^{1}H NMR shifts of **16**, *iso*-**16**, and **22** (positional numbers analogous to **1**–**3**).



	16	*iso*-**16**	**22**
2-H	6.18	5.97–6.21[a]	6.18
3-H	7.37	7.35	7.37
5-H	5.81	5.80	5.82
6-H	6.79	6.67	6.80
7-H	6.06	5.97–6.21[a]	6.06
8-H_{1or2}	4.34	2.36–2.54[b]	4.24
9-H_{1or2}	δ_A=2.39	4.21	δ_A=2.41
	δ_B=2.50		δ_B=2.59
10-H_{0or1}	5.93	5.97–6.21[a]	–
11-H_{1or2}	6.11	5.97–6.21[a]	*Z*-H 5.36
			E-H 5.81

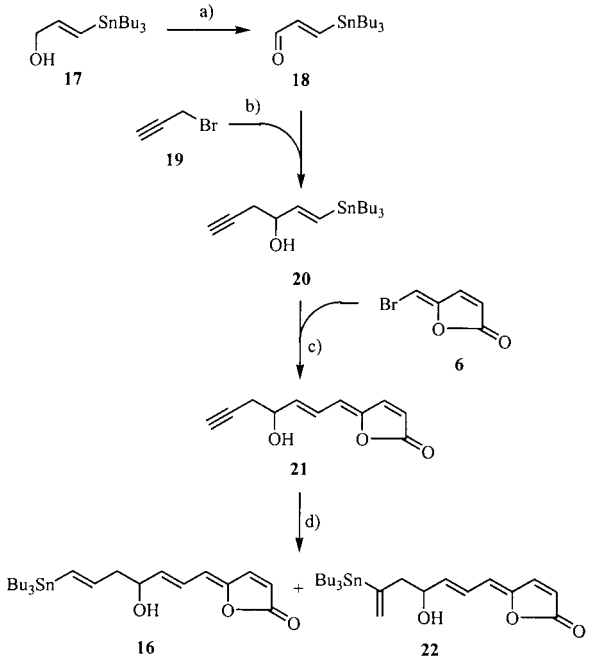
[a] Overlapping signal of four protons of *iso*-**16** and 2 protons of **16**. [b] Overlapping with signals of $\mathbf{16}_{9\text{-}H_2}$.

The synthesis of the siloxylated type-**4** enediyne **27** began with the synthesis of enediynol **25** from epichlorohydrin and lithiobutadiyne (Scheme 6). The latter was generated in situ from dichlorobutyne (**23**) and excess lithium amide.[30] This reaction established the backbone and functional groups of heptenediynol **25** in a single operation albeit only 17% yield. O-Silylation[31] (→**26**) and C-iodination[32] (→**27**) followed with 75 and 87% yield, respectively.

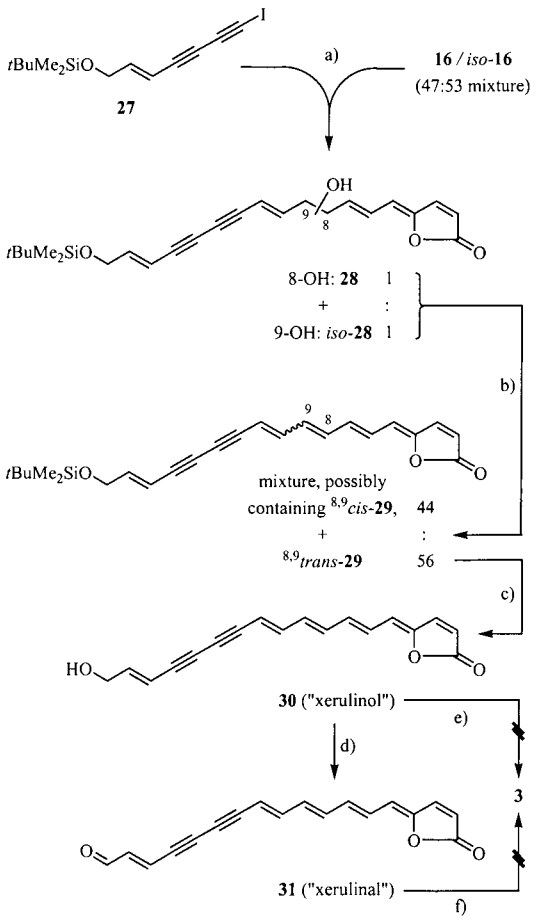


Scheme 6. Synthesis of the first type-**4** diyne fragment. a) $LiNH_2$ (6.0 equiv), NH_3 (l), −40°C; addition of **24** (0.5 equiv), 3.5 h; → RT, 12 h; 17%. b) *t*$BuMe_2SiCl$ (1.0 equiv), imidazole (2.0 equiv), CH_2Cl_2, 0°C, 2 h; 75%. c) BuLi (1.2 equiv), THF, −78°C, 5 min; I_2 (1.2 equiv), −78°C, 25 min, RT, 15 min; 87%.

Scheme 7 depicts how we advanced from the enediynol **25** and the mixture of monocoupling products **16** and *iso*-**16** to the alcohol analogue **30** ("xerulinol") and aldehyde analogue **31** ("xerulinal") of xerulinic acid (**3**). Pd-mediated coupling between the starting materials gave 51% of an inseparable 1:1 mixture of isomers **28** and *iso*-**28**.[33] We returned to working with single isomers compounds after the subsequent dehydration: Treatment of the 1:1 mixture **28**/*iso*-**28** with triflic anhydride and triethylamine allowed to



Scheme 5. a) Dess–Martin periodinane (1.3 equiv), CH_2Cl_2, 0°C → RT, 2.5 h; 93%. b) **19** (1.0 equiv), Mg (1.5 equiv), $HgCl_2$ (2 mol%), Et_2O, 0°C, 90 min; **18**, −10°C, 10 min, 0°C, 1 h; 68%. c) $[Pd(dba)_2]$ (4 mol%), $AsPh_3$ (12 mol%), THF, RT, 2 h; 73%. d) Bu_3SnH (1.20 equiv), $[PdCl_2(PPh_3)_2]$ (2 mol%), THF, RT, 30 min; 36% **16** and 37% **22** (separated).

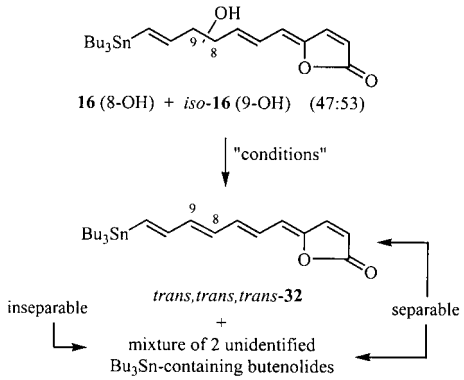


Scheme 7. Syntheses of "xerulinol" and "xerulinal". a) **27** (1.5 equiv), $[Pd(dba)_2]$ (5 mol%), $AsPh_3$ (20 mol%), THF, RT, 24 h; 51%. b) NEt_3 (5.0 equiv), Tf_2O (1.5 equiv), CH_2Cl_2, −78°C → −20°C, 2 h; 48% ^{8,9}*trans*-**29** separated from 39% of the indicated mixture. c) HF/pyridine (134.1 equiv), THF, 0°C, 5 h, <67%. d) Dess–Martin periodinane (1.2 equiv), CH_2Cl_2, RT, 1 h; >64%; 43% over the two steps. e) Stream of O_2, AcOEt, cat. PtO_2; no reaction. f) CrO_3 (2.0 equiv), H_2SO_4, acetone; decomp.; or $NaClO_2$ (1.5 equiv), KH_2PO_4 (5.0 equiv), H_2O_2 (1.6 equiv), H_2O/acetone; no reaction; or O_2, CH_2Cl_2, $RuCl_3$ (0.1 equiv); no reaction.

isolate the desired all-*trans*-configured elimination product ^{8,9}*trans*-**29** (48%) after chromatographic separation from unassigned "isomers" (39%; possibly containing compound ^{8,9}*cis*-**29**). Desilylation of ^{8,9}*trans*-**29** with HF/pyridine complex[34] and Dess–Martin oxidation[27] led to "xerulinol" and "xerulinal" successively (43% yield over the two steps). Disappointingly, under a variety of conditions we couldn't oxidize either of these compounds to obtain xerulinic acid—plausibly because "xerulinal" was very unstable and readily decomposed giving black unidentified materials.

Our failure of adjusting the oxidation state of the sidechain of butenolide **31** from "carbonyl" to "carboxyl" implied that we should work with the correct oxidation state from earlier on. Consequently, we switched to incorporating the enediyne *ester* **44** (to be presented in Scheme 10) instead of the enediyne *ether* **27** (Scheme 7) as a type-**4** reagent. However, we did not engender **44** in an approach paralleling that of Scheme 7—because of the lack of *trans*-selectivity of *its* dehydration step (**28**/*iso*-**28** → ^{8,9}*cis*- and ^{8,9}*trans*-**29**). Rather we considered the stannylated heptatrienylidenebutenolide *trans*,*trans*,*trans*-**32** as an ideal coupling partner of enediyne ester **44**. However, through dehydration compound *trans*,*trans*,*trans*-**32** wasn't accessible in good yields, either (Table 2).

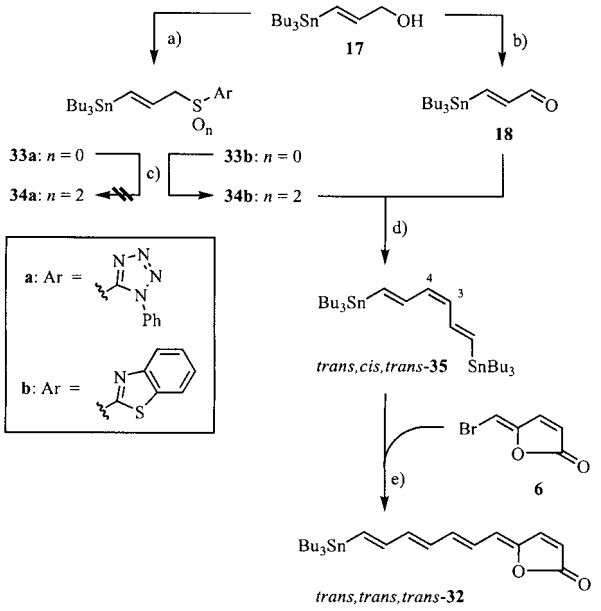
Table 2. Dehydration of 1:1 mixtures **16**/*iso*-**16**.



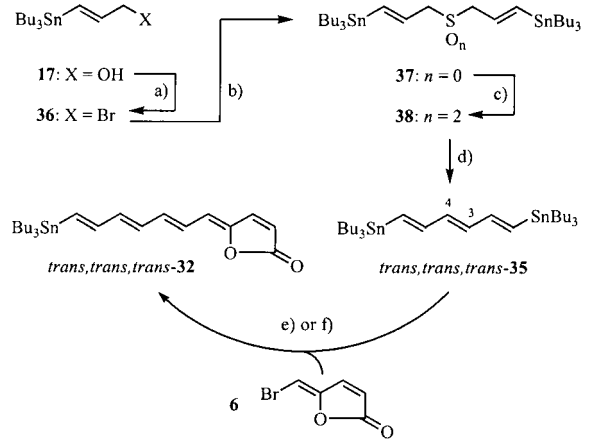
Reagents	Solvent	*T* [°C]	Yield [%] *trans*,*trans*,*trans*-**32**	Yield [%] "mixture"
DEAD/PPh_3	CH_2Cl_2	−35→0	decomp.	–
Ac_2O/DBU/DMAP	CH_2Cl_2	−35→0	9	–
Ms_2O/Hünig's base	CH_2Cl_2	0	10	–
MsCl/NEt_3/DMAP	THF	0	decomp.	–
Tf_2O/pyridine	CH_2Cl_2	−78→−30	30	7
Tf_2O/NEt_3	CH_2Cl_2	−78→−30	41	11

This let us approach the same butenolide differently: by mono-Stille couplings between (bromomethylene)butenolide **6** and the through-conjugated bis(stannanes) *trans*,*cis*,*trans*-**32** (Scheme 8) or *trans*,*trans*,*trans*-**32** (Scheme 9). Each of these couplings afforded the desired *trans*,*trans*,*trans*-isomer of butenolide **32** with 100% stereocontrol. The former reaction revealed *trans*,*trans*,*trans*-selectivity as a surprise, the latter by design.

The bis(stannylated) hexatriene *trans*,*cis*,*trans*-**35** was assembled from the tin-containing alcohol **17** (Scheme 8), itself accessible through cuprostannylation/protonolysis from propargyl alcohol.[26] We divided alcohol **17** between a Dess–Martin oxidation[27] (→ 93% aldehyde **18**[28]) and two Mukaiyama redox condensations delivering sulfides **33a** (92%) and **33b** (96%).[35] The latter, in contrast to the former, could be oxidized with peroxomolybdate,[36] forming sulfone **34b** (83% yield). Deprotonation with KHMDS in the presence of aldehyde **18** effected a (Sylvestre) Julia olefination[37]—that is, a one-step variant of the (Marc) Julia–Lythgoe olefination. It furnished bis(stannane) **35** in 66% yield[38] as a 96:4 mixture of isomers. From this degree of selectivity we concluded—understandably[39]—that the 96% constituent was the *trans*,*trans*,*trans*-isomer. To our surprise, the SELINCOR pulse sequence[40] revealed that this isomer was *trans*,*cis*,*trans*-configured since the coupling $J_{3,4}$ between



Scheme 8. Stereoselective synthesis I of key intermediate *trans,trans,-trans*-**32**. a) **33a**: Diethyl azodicarboxylate (1.09 equiv), PPh_3 (1.10 equiv), 1-phenyl-1*H*-tetrazole-5-thiol (1.06 equiv), THF, 0 °C, 3 h; 92 %; **33b**: Diethyl azodicarboxylate (1.09 equiv), PPh_3 (1.10 equiv), benz-1,3-thiazole-2-thiol (1.05 equiv), THF, 0 °C, 1 h; 96 %. b) Same as a) in Scheme 5. c) H_2O_2 (10 equiv), $(NH_4)_6Mo_7O_{24}$ (0.20 equiv), EtOH, 0 °C, 2 h; 83 %. d) KHDMS (1.2 equiv), THF, −78 °C → RT, 12 h; 66 %. e) **6** (1.0 equiv), $[Pd(dba)_2]$ (5 mol %), $AsPh_3$ (20 mol %), CuI (10 mol %), THF, 40 °C, 2 h; 55 %.



Scheme 9. Stereoselective synthesis II of key intermediate *trans,trans,-trans*-**32**. a) CBr_4 (1.21 equiv), CH_2Cl_2, 0 °C, addition of PPh_3 (1.10 equiv), 1 h; 82 % (ref.[44] 81 %). b) Na_2S (0.5 equiv), $Bu_4N^+HSO_4^-$ (0.7 mol %), H_2O/THF, RT, 7 h; 90 %. c) H_2O_2 (10 equiv), $(NH_4)_6Mo_7O_{24}$ (0.2 equiv), EtOH, 0 °C → RT, 1 h; 88 %. d) KOH (30 % on Al_2O_3; 20 equiv), CBr_2F_2 (4 equiv), THF, 0 °C, 30 min; 73 %. e) *trans,trans,trans*-**35** (1.3 equiv), *n*BuLi (1.3 equiv), THF, −78 °C, 20 min; $ZnCl_2$ (1.3 equiv), 30 min; **6**, $[Pd(PPh_3)_4]$ (5 mol %), 0 °C, 1 h; 63 %. f) **6** (1.1 equiv), $[Pd(dba)_2]$ (5 mol %), $AsPh_3$ (20 mol %) THF, RT, 2 h; 44 %.

the central protons was 10.9 Hz (a value inaccessible from standard ^{1}H NMR spectra because it refers to the coupling between protons of identical chemical shifts). As we have established since,[41] (Sylvestre) Julia olefinations of other aldehydes than compound **18** with sulfone **34b** and KHMDS as a base exhibit comparable degrees of *cis* selectivity.

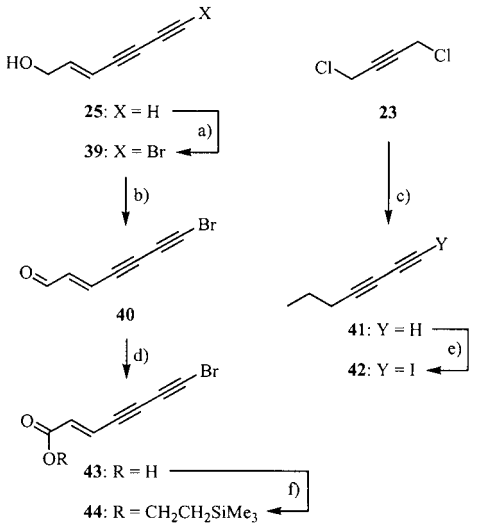
Notwithstanding the wrong double bond configuration of bis(stannane) *trans,cis,trans*-**35**, we attempted pushing on towards xerulinic acid by performing a Stille coupling[9] with 1.0 equivalent of butenolide **6** in the presence of $[Pd(dba)_2]$/$AsPh_3$/CuI[42] (bottom of Scheme 8). This provided 55 % of a single mono-coupling product to which we assigned structure *trans,trans,trans*-**32**. What formerly had been protons 3 and 4 of bis(stannane) *trans,cis,trans*-**35** were now protons 8 and 9. Having different chemical shifts, protons 8 and 9 of butenolide *trans,trans,trans*-**32** display their coupling with one another already in the ordinary ^{1}H NMR spectrum. The value $J_{8,9}=14.7$ Hz established that this C=C bond possesses the desired *trans*-configuration. We have no clue as to why or how this complete inversion of the crucial C=C bond configuration came about during the transformation **35** + **6** → **32**.[43] In any event, it served us well and reproducibly.

Scheme 9 shows a stereochemically *rational* approach to the previously obtained butenolide *trans,trans,trans*-**32**. It proceeds via bis(stannane) *trans,trans,trans*-**35**. Like its *trans,cis,trans*-isomer (cf. Scheme 8), this reagent was derived from compound **17**[26] (Scheme 9). In the present context, this tin-containing alcohol was converted via the tin-containing bromide **36** (82 %)[44] into the tin-containing sulfide **37** (90 %).[45] Oxidation with peroxomolybdate provided the corresponding sulfone **38** (88 %).[36] Deprotonation with Al_2O_3-supported KOH in the presence of CBr_2F_2[46] induced a Ramberg–Bäcklund reaction.[47] Bis(stannane) **35** resulted in 73 % yield. It represented a 96:4 mixture of the *trans,trans,-trans*- and the *trans,cis,trans*-isomer. This was inferred from the ratio of the integrals over 2-H/5-H (*trans,trans,trans*-**35**: $\delta_{2\text{-H}}=\delta_{5\text{-H}}=6.56$, *trans,cis,trans*-**35**: $\delta_{2\text{-H}}=\delta_{5\text{-H}}=7.08$) and from the magnitudes of the vicinal olefinic H,H coupling constants in the major isomer ($J_{1,2}=J_{5,6}=18.6$ Hz, $J_{3,4}=15.1$ Hz; the latter was determined in a SELINCOR experiment[40]).

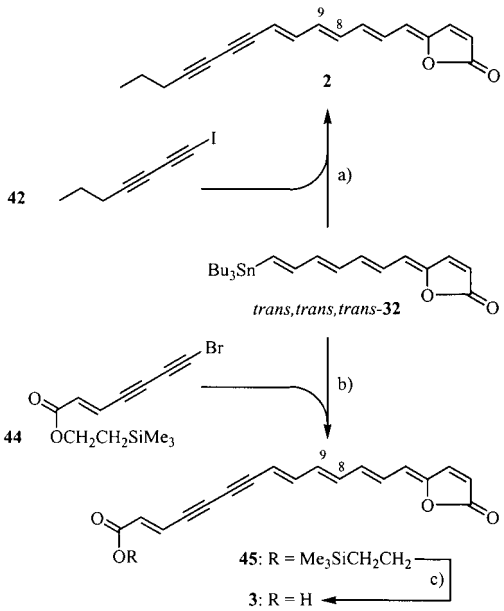
In order to couple bis(stannane) *trans,trans,trans*-**35** and (bromomethylene)butenolide **6** in a 1:1 ratio without too much 1:2 coupling competing, we performed one Sn→Li exchange per reagent molecule first, a Li→Zn exchange next, and a Negishi coupling[48] thereafter. This led to the desired 1:1 product *trans,trans,trans*-**32** in 63 % yield (Scheme 9).[49] The prefixes "*trans*" are founded on the magnitude of the following H,H coupling constants (500 MHz, $CDCl_3$): $J_{6,7}=14.9$, $J_{8,9}=14.7$, and $J_{10,11}=18.7$ Hz.

It is noteworthy that we were able to couple *different* electrophiles at terminus C^1 versus C^6 of our bis(tributylstannanes) *trans,cis,trans*- and *trans,cis,trans*-**35** (Schemes 8 and 9, respectively). These differentiations are more challenging than realizing the C^1- versus C^4-differentiation in the only unsymmetric biscoupling reported so far for the conceptionally related butadiene-1,4-bis(trimethylstannane).[50a]

The synthesis of the type-**4** enediynecarboxylate **44** began with enediynol **25** (Scheme 10). Terminal bromination with NBS/$AgNO_3$[51] led to bromoenediynol **39**. The correspond-



Scheme 10. Syntheses of second and third type-**4** diyne fragments. a) NBS (1.30 equiv), $AgNO_3$ (0.08 equiv), acetone, RT, 13 h; 79%. b) Dess–Martin periodinane (1.52 equiv), CH_2Cl_2, 0°C → RT, 2.5 h; 79%. c) Ref.[3] $NaNH_2$ (3.0 equiv), NH_3/DMSO (6:1), −33°C; PrBr (1.1 equiv), 4 h; used crude. d) $NaClO_2$ (2.1 equiv), KH_2PO_4 (2.5 equiv), 2-methyl-2-butene (3.5 equiv), acetone/H_2O 3:2, 0°C; 89%. e) Ref.[3] I_2 (1.0 equiv), morpholine (3.0 equiv), THF, 45°C, 10 h; 43% over the two steps. f) $HOCH_2CH_2SiMe_3$ (1.2 equiv), DCC (1.1 equiv), DMAP (0.05 equiv), ethyl acetate, 0°C → RT, 2 h; 83%.



Scheme 11. a) **42** (1.8 equiv), [Pd(dba)$_2$] (5.3 mol%), $AsPh_3$ (17.3 mol%), CuI (11.1 mol%), THF, RT, 5 h; 70%. b) **44** (1.08 equiv), [Pd(dba)$_2$] (6 mol%), $AsPh_3$ (19 mol%), THF, RT, 5 h; 73%. c) Bu_4NF (1.5 equiv), THF, 0°C → RT, 2 h; 61%.

ing aldehyde **40** was generated by Dess–Martin oxidation[27] (79% yield). This aldehyde was carried on to carboxylic acid **43** by a Lindgren oxidation[52] (89% yield). Esterification with (trimethylsilyl)ethanol in the presence of DCC and DMAP provided 83% of building block **44**.[53]

The synthesis of another type-**4** reagent—namely of iododiyne **42**—was required for enriching the present study by a completely stereoselective synthesis of dihydroxerulin (**2**), too. Following a procedure of ourselves,[3] we started with the earlier mentioned (Scheme 6) generation of lithiobutadiyne from dichlorobutyne (**23**) and excess lithium amide (Scheme 10).[30] Quenching with propyl bromide gave a crude specimen of 1,3-heptadiyne (**41**). It was iodinated at C-1 by treatment with iodine and morpholine at slightly elevated temperature,[54] affording compound **42** in 43% yield over the two steps.

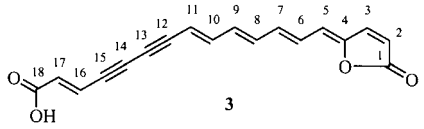
The carbon skeleton of xerulinic acid (**3**) was completed by a Stille coupling[33] {[Pd(dba)$_2$]/$AsPh_3$[55]} between the brominated enediynecarboxylate **44** and the tin-containing butenolide *trans,trans,trans*-**32** (Scheme 11). Avoiding exposure to atmospheric oxygen and daylight, this provided xerulinic acid ester **45** in 73% yield. In the final step, this compound was deprotected in 61% yield by treatment with anhydrous Bu_4NF in THF. The resulting synthetic specimen of xerulinic acid showed the same ^{1}H- and ^{13}C- and 2D-NMR data as the natural product[2,56] (Table 3; 500 and 126 MHz, respectively). A ^{1}H-coupled short-range H,C-COSY spectrum (500 MHz/125.7 MHz, [D$_6$]DMSO) showed $J_{9,8}$ = 14.7 Hz (along with $J_{9,10}$ = 11.0 Hz) in the ^{13}C-9 signal (δ = 134.70) and $J_{8,9}$ = 14.9 Hz (as well as $J_{8,7}$ = 11.2 Hz) in the ^{13}C-8 signal (δ = 137.57). These values average 14.8 Hz for the olefinic coupling across the C^8=C^9 bond of xerulinic acid and proves the *trans*-configuration (established by Steglich, Anke et al. by analyzing ^{1}H NMR spectra in [D$_6$]DMSO/[D$_6$]benzene mixtures[2]).

Likewise, dihydroxerulin (**2**) was obtained by the Stille coupling[33] {[Pd(dba)$_2$]/$AsPh_3$/CuI[42]} of the iodinated diyne **42** with the stannylated heptatrienylidenebutenolide *trans,-trans,trans*-**32** (Scheme 11), namely in 70% yield and—other than in our original synthesis[3]—without another stereoisomer interfering. In our earlier study,[3] we needed to simulate the 800 MHz 8-H/9-H ^{1}H NMR subspectrum of dihydroxerulin (**2**) in C_6D_6—which was higher-order—for unraveling $J_{8,9}$ = 14.8 Hz and thereby establishing the *trans*-configuration of the C^8=C^9 bond of **2**. This time, we extracted $J_{8,9}$ = 14.9 Hz—as the average value of the 15.2 and 14.6 Hz splittings, respectively, observed in the ^{13}C resonances at δ = 135.69 and 134.77 (C-8, C-9; not individually assigned)—directly from the ^{1}H-coupled short-range H,C-COSY spectrum (500 MHz/125.7 MHz, [D$_6$]benzene).

In summary, we realized a highly convergent and highly stereoselective first-time synthesis of xerulinic acid (**3**) and accomplished an equally convergent and equally stereoselective synthesis of dihydroxerulin (**2**). While these targets are maybe no "complex" molecules it must be pointed out that they are by no means easy to make: Their tendency—and the tendency of several of their precursors—to "polymerize" cannot be overestimated.

Our strategy towards **2** and **3** is distinct from all previous strategies in the xerulin field. Both compounds were derived from three building blocks, namely from the halogenated diynes **42** or **44**, respectively, either of the novel bis(stan-

Table 3. ^{1}H (500 MHz) and ^{13}C NMR (126 MHz) chemical shifts of natural and synthetic xerulinic acid (**3**; [D$_6$]DMSO). For the corresponding data of natural and synthetic dihydroxerulin (**2**) see reference [3].



3

Proton	Natural	Synthetic	Carbon	Natural	Synthetic
–			1	169.10	169.04
2	6.43	6.43	2	118.77	118.75
3	7.84	7.85	3	144.32	144.26
–			4	149.63	149.61
5	6.25	6.25	5	114.45	114.38
6	6.85	6.70	6	128.38	128.37
7	6.73	–	7	138.08	138.02
8	6.74	6.82	8	137.47	137.57
9	6.63	6.60–6.68	9	134.77	134.70
10	6.99	7.00	10	146.41	146.45
11	6.08	6.08	11	110.36	110.27
–			12	85.68	85.86
–			13	77.45	77.34
–			14	80.93	80.88[c]
–			15	81.11	81.26[c]
16	6.87[a]	6.82	16	121.97	122.63
17	6.48[a]	6.42	17	135.73[b]	134.80
–			18	166.14	165.94

[a] A copy of the original ^{1}H NMR spectrum revealed that this (published) value is a typographical error; the actually observed chemical shift value was at higher field. [b] The original ^{13}C NMR spectra show $\delta = 135.73$ (published) and $\delta = 135.17$. [c] Assignments may be interchangeable.

nanes) *trans*,*cis*,*trans*- or *trans*,*trans*,*trans*-**35**, and the easily accessible (bromomethylene)butenolide **6**.

The hexatriene-1,6-bis(tributylstannanes) *trans*,*cis*,*trans*- and *trans*,*cis*,*trans*-**35** ought to be valuable conjunctive C_6 reagents—the first examples being provided in the present study (Schemes 8 and 9, respectively)—, similarly as ethylene-1,2-bis(tributylstannane) which is a conjunctive C_2 reagent[57] or similarly as butadiene-1,4-bis(trimethylstannane) which is a conjunctive C_4 reagent.[50,58] Pertinent studies are underway in our laboratory. The (bromomethylene)butenolide **6** in conjunction with the concise synthesis disclosed here should make it a worthwhile precursor for the synthesis of other γ-alkylidenebutenolides, too. Thus, the target-oriented work reported here entails methodological innovation of a wider scope.

Experimental Section

All reactions were performed in oven-dried (110 °C) glassware under Ar. Reactions with light-sensitive compounds were performed in brown glassware or in ordinary glassware in a fume hood lined with UV protection foil. THF was freshly distilled from K; CH_2Cl_2 and pyridine were distilled from CaH_2. Products were purified by flash chromatography[29] on Merck silica gel 60 [eluents in brackets; volume of each collected fraction (mL)/column diameter (cm): 1.3/1.0, 4/1.5, 8/2.0, 14/2.5, 14(!)/3.0, 30/4, 50/5, 80/6; which fractions contained the isolated product is indicated in each description as "product in *xx*–*yy*"]. Yields refer to analytically pure samples. Isomer ratios were derived from suitable ^{1}H NMR integrals. ^{1}H [$CHCl_3$ ($\delta = 7.26$) as internal standard in $CDCl_3$, C_6HD_5 ($\delta = 7.15$) as internal standard in C_6D_6 or $(HD_2C)(D_3C)S{=}O$ ($\delta = 2.49$) as internal standard in $(CD_3)_2S{=}O$] and ^{13}C NMR [$CDCl_3$ (center peak of the triplet $\delta = 77.0$) as internal standard in $CDCl_3$, C_6D_6 ($\delta = 128.0$) as internal standard in C_6D_6 or $(D_3C)_2S{=}O$ ($\delta = 39.5$) as internal standard in $(D_3C)_2S{=}O$]: Varian Mercury VX 300, Bruker AM 400 and Bruker DRX 500. Integrals in accordance with assignments; coupling constants in Hz. The assignments of ^{1}H and ^{13}C NMR resonances refer to the IUPAC nomenclature and printed numbers belong to the side chain [except for dihydroxerulin, xerulinic acid 2-(trimethylsilyl)ethyl ester, and xerulinic acid, which were numbered as shown for the latter in Table 3]. Combustion analyses: E. Hickl, Institut für Organische Chemie und Biochemie, Universität Freiburg. MS: Dr. J. Wörth und C. Warth, Institut für Organische Chemie und Biochemie, Universität Freiburg. IR spectra: Perkin–Elmer Paragon 1000. Melting points were measured on a Dr. Tottoli apparatus (Büchi) and are uncorrected.

Dihydroxerulin (2): To a degassed solution of stannane *trans*,*trans*,*trans*-**32** (63.5 mg, 0.137 mmol) in THF (1.5 mL) [Pd(dba)$_2$] (4.2 mg, 7.3 μmol, 0.053 equiv), $AsPh_3$ (7.3 mg, 24 μmol, 0.17 equiv), CuI (2.9 mg, 15 μmol, 0.11 equiv), and iodoalkyne **42** (67.0 mg, 0.250 mmol, 1.82 equiv) were added. After stirring for 5 h under exclusion of light the solvent was evaporated in vacuo to afford a residue which was purified by flash chromatography (2.5 cm, cyclohexane/EtOAc 10:1, #11–23 cyclohexane/EtOAc 5:1, #24–25 cyclohexane/EtOAc 2:1, product in #19–25) to afford the title compound (25.2 mg, 70 %) as an orange solid; ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz, C_6D_6), and IR spectrum similar to data published earlier.[3] $J_{8,9}$ was obtained by an ^{1}H-coupled short-range C,H correlation spectrum: 1) The signal at $\delta = 134.77$ (C-8) is split by $J = 14.6$ and $J' = 11.7$ → the *larger* one of these couplings is $J_{8,9}$. 2) The signal at $\delta = 135.69$ (C-9) is only interpretable without simulation in the high-field part, where it is split by $J = 15.2$ and $J' = 11.5$ → the *larger* one of these couplings is $J_{9,8}$.

Xerulinic acid (3): At 0 °C $Bu_4N^+F^-$ (1.0 M in THF, 161 μL, 0.161 mmol, 1.10 equiv) was added under light exclusion within 1 min to a solution of ester **44** (57.2 mg, 0.146 mmol) in THF (2 mL). The solution was allowed to warm to room temperature within 2 h. More $Bu_4N^+F^-$ (1.0 M in THF, 58 μL, 0.058 mmol, 0.40 equiv) was added. After 2 h EtOAc (6 mL), H_2O (4 mL), and aq. NH_4Cl (1 mL) were added. The aq. phase was extracted with EtOAc (4×4 mL) and the combined organic phases were washed with brine (2×2 mL). After drying with Na_2SO_4 the solvent was evaporated in vacuo to afford a residue which was purified by flash chromatography (2×3 cm, 4 mL fractions, EtOAc, product in #16–48) to afford the title compound (26.0 mg, 61 %) as an orange solid. ^{1}H NMR (500 MHz, [D$_6$]DMSO): $\delta = 6.08$ (d, $J_{11,10} = 15.5$, 11-H), 6.25 (d, $J_{5,6} = 10.9$, 5-H), 6.42 (d, $J_{17,16} = 15.8$, 17-H), interlocked with 6.43 (d, $J_{2,3} = 5.2$, 2-H), 6.60–6.68 (m, 9-H), 6.70–6.82 (m, 6-H, 7-H, 8-H), superimposes partly 6.82 (dd, $J_{16,17} = 15.8$, $^7J_{16,11} = 0.9$, 16-H), 7.00 (dd, $J_{10,11} = 15.4$, $J_{10,9} = 11.2$, 10-H), 7.85 (d, $J_{3,2} = 5.4$, 3-H); a short-range H,H correlation spectrum (500 MHz, [D$_6$]DMSO) showed, amongst others, cross-peaks between the following resonances: 5-H ($\delta = 6.25$) ⇔ 6-H, 7-H, 8-H ($\delta = 6.70$–6.82); 11-H ($\delta = 6.08$) ⇔ 10-H ($\delta = 7.00$), 16-H ($\delta = 6.82$); 10-H ($\delta = 7.00$) ⇔ 9-H ($\delta = 6.60$–6.68), 9-H ($\delta = 6.60$–6.68) ⇔ 10-H ($\delta = 7.00$), 6-H, 7-H, 8-H ($\delta = 6.70$–6.82); ^{13}C NMR (125 MHz, [D$_6$]DMSO): $\delta = 77.34$ (C-13), 80.88 (C-14)*, 81.26 (C-15)*, 85.86 (C-12), 110.27 (C-11), 114.38 (C-5), 118.75 (C-2), 122.63 (C-16), 128.37 (C-6), 134.70 (C-9), 134.80 (C-17), 137.57 (C-8), 138.02 (C-7), 144.26 (C-3), 146.45 (C-10), 149.61 (C-4), 165. 94 (C-18), 169.04 (C-1); *assignment (different from Steglich et al.[2]) by long-range C,H correlation and ^{1}H-coupled ^{13}C NMR spectrum. A short-range C,H correlation spectrum (500 MHz/125 MHz, [D$_6$]DMSO) showed cross-peaks between the following resonances: 11-H ($\delta = 6.08$) ⇔ C-11 ($\delta = 110.27$), 5-H ($\delta = 6.25$) ⇔ C-5 ($\delta = 114.38$), 17-H ($\delta = 6.42$) ⇔ C-17 ($\delta = 134.80$)*, 2-H ($\delta = 6.43$) ⇔ C-2 ($\delta = 118.75$)*, 9-H ($\delta = 6.60$–6.68) ⇔ C-9 ($\delta = 134.70$), 6-H, 7-H, 8-H ($\delta = 6.70$–6.82) ⇔ C-6, C-7, C-8 ($\delta = 128.37$, 137.57 and 138.02), 16-H ($\delta = 6.82$) ⇔ C-16 ($\delta = 122.63$), 10-H ($\delta = 7.00$) ⇔ C-10 ($\delta = 146.45$), 3-H ($\delta = 7.85$) ⇔ C-3 ($\delta = 144.26$); *since the signals of 2-H and 17-H are superimposed, the cross-peaks to C-2/C-17 had to be distinguished by "narrow" (→ 2-H) vs. "broad" (→ 17-H due to its *larger* H,H coupling). An ^{1}H-coupled ^{13}C NMR spectrum (125 MHz, [D$_6$]DMSO) revealed, amongst others: The "inner" alkyne ^{13}C signals at

$\delta = 77.34$ and $\delta = 81.26$ occurred as t while the "outer" alkyne ^{13}C signals at $\delta = 80.88$ (C-15) and $\delta = 85.86$ (C-12) occurred as d. A long-range C,H correlation spectrum (500 MHz/125 MHz, [D_6]DMSO) showed, amongst others, cross-peaks between the following resonances: 2-H ($\delta = 6.20$) $\Leftrightarrow$ C-3 ($\delta = 142.53$), C-4 ($\delta = 149.73$), C-1 ($\delta = 169.18$), 10-H ($\delta = 7.00$) $\Leftrightarrow$ C-9 ($\delta = 134.70$), C-8 ($\delta = 137.57$), 9-H ($\delta = 6.60$–6.68) $\Leftrightarrow$ C-8 ($\delta = 137.57$), C-7 ($\delta = 138.02$), 10-H ($\delta = 7.00$) $\Leftrightarrow$ C-12 ($\delta = 85.86$), 11-H ($\delta = 6.08$) $\Leftrightarrow$ C-13 ($\delta = 77.34$), C-14 ($\delta = 81.26$), 17-H ($\delta = 6.42$) $\Leftrightarrow$ C-15 ($\delta = 80.88$), C-14 ($\delta = 81.26$). 3-H ($\delta = 7.85$) $\Leftrightarrow$ C-2 ($\delta = 118.75$), C-4 ($\delta = 149.26$), C-1 ($\delta = 165.95$). A ^1H-coupled short-range C,H correlation spectrum (500 MHz/125 MHz, [D_6]DMSO) revealed, amongst others: $\delta = 6.41$ (dd, $^1J_{H,C} = 167.3$, $J_{17,16} = 16.1$, 17-H), $\delta = 6.43$ (dd, $^1J_{H,C} = 186.3$, $J_{2,3} = 5.5$, 2-H), $\delta = 6.64$ (only partly interpretable $J_{9,8} = 14.7$, $J_{9,10} = 11.0$, 9-H), $\delta = 6.74$ (ddd, $^1J_{H,C} = 158.5$, $J_{7,6} = 14.8$, $J_{7,8} = 11.3$, 7-H), $\delta = 6.75$ (only partly interpretable, $J_{8,9} = 14.9$, $J_{8,7} = 11.2$, 8-H), $\delta = 6.79$ (ddm, $^1J_{H,C} = 159.6$, $J_{6,7} \approx 14.5$, $J_{6,5} \approx 11.5$, 6-H); IR ([D_6]DMSO): $\tilde{\nu} = 3465$, 3025, 2250, 2185, 2130, 1770, 1745, 1700, 1610, 1530, 1330, 1290, 1265, 1190, 1110, 1095, 1030, 985, 935, 880, 835, 805 cm^{-1}; (m/z): 292.07356 [M^+] confirmed by HRMS (EI, 70 eV); elemental analysis calcd (%) for $C_{18}H_{12}O_4$ (292.1): C 73.97, H 4.14; found: C 73.61, H 4.07.

***trans,trans*-1,6-Bis(tributylstannyl)-1,5-hexadien-3-ol (5)**: AIBN (534 mg, 3.26 mmol, 0.18 equiv) was added to a solution of diyne **15** (1.463 g, 17.95 mmol) and Bu_3SnH (13.150 g, 45.190 mmol, 2.52 equiv) in toluene (9 mL). The solution was stirred 4 h at 80 °C, then 11 h at room temperature The solvent was removed in vacuo and the residue purified by flash chromatography (5.5 cm, cyclohexane/NEt_3 100:2, product in #15–25) to yield the title compound (7.269 g, 60 %) as a slightly yellow oil; ^1H NMR (500 MHz, $CDCl_3$; contaminated with a small amount of Bu_3SnX): $\delta =$ 0.81–0.96 (m, 6 × SnCH_2CH$_2$CH$_2$CH$_3$), superimposes 0.89 (t, $J_{vic} = 7.2$, 6 × SnCH$_2$CH$_2$CH$_2$CH$_3$), 1.23–1.37 (m, 6 × SnCH$_2$CH$_2$CH_2CH$_3$), 1.43–1.53 (m, 6 × SnCH$_2$CH_2CH$_2$CH$_3$), 1.72 (d, $J_{OH,3\text{-}H} = 4.5$, OH), 2.40 [m, presumably interpretable as AB signal ($\delta_A = 2.36$, $\delta_B = 2.45$, $J_{AB} = 13.7$, in addition split by $J_{A,3} = J_{A,5} = 6.9$, $^4J_{A,6} = 0.9$, $J_{B,3} = 6.3$*, $J_{B,5} = 5.1$*, $^4J_{B,6} = 1.1$, 4-H_2), 4.14 (m, 3-H), 5.90–6.26 (m, 1-H, 2-H, 5-H, 6-H); *interchangeable; ^{13}C NMR (75 MHz, $CDCl_3$; peak of contaminant at $\delta = 10.31$): $\delta = 9.46$ (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1'} = {}^1J_{^{119}Sn,C\text{-}1''} = 344.0$, $^1J_{^{117}Sn,C\text{-}1'} = {}^1J_{^{117}Sn,C\text{-}1''} = 327.6$, Sn$CH_2CH_2CH_2CH_3$), 13.69 SnCH$_2CH_2CH_2$-$CH_3$), 27.24 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3'} = {}^3J_{^{119}Sn,C\text{-}3''} = {}^3J_{^{117}Sn,C\text{-}3'} = {}^3J_{^{117}Sn,C\text{-}3''} = 53.8$, SnCH$_2CH_2CH_2CH_3$), 29.055 and 29.101 (2 × non equivalent SnCH$_2$CH$_2$CH$_2$CH$_3$), 45.93 (C-4), 73.73 (C-3), 127.52, 132.90, 144.44, 150.13 (C-1, C-2, C-5, C-6); IR (film): $\tilde{\nu} = 3340$, 2955, 2925, 2870, 2850, 1600, 1460, 1420, 1375, 1355, 1340, 1290, 1250, 1180, 1150, 1075, 1045, 1020, 990, 960, 875 cm^{-1}; elemental analysis calcd (%) for $C_{30}H_{62}OSn_2$ (674.3): C 53.28, H 9.24; found: C 53.46, H 9.15.

***Z*-5-(Bromomethylene)-2(5*H*)-furanone (6)**: *Method A*: 5-Bromolevulinic acid methyl ester (**9**; 724 mg, 5.46 mmol) was treated with conc. H_2SO_4 (7 mL) and stirred for 20 min at 100 °C. After cooling down, the mixture was poured on ice and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with brine (20 mL), dried with Na_2SO_4, and exaporated in vacuo. The residue was purified by chromatography (2 cm, cyclohexane/EtOAc 15:1, #5–9 cyclohexane/EtOAc 10:1, #10–24 cyclohexane/EtOAc 5:1, product in #17–24). The title compound (119.0 mg, 20 %) was obtained as a colorless solid. M.p. 83–84 °C.

Method B: Bu_3SnH (127.0 mg, 439.9 μmol, 1.10 equiv) was added to a degassed solution of dibromide **10** (101.4 mg, 399.5 μmol) and [$Pd(PPh_3)_4$] (46.0 mg, 39.9 μmol, 0.10 equiv) in THF (3 mL). The mixture was stirred for 3 h at 60 °C. After cooling to room temperature, the mixture was filtered through a pad of Celite and washed thoroughly with EtOAc. The solvent was evaporated in vacuo affording a residue which was purified by repeated flash chromatography (2 cm, cyclohexane/EtOAc 10:1, #4–8 cyclohexane/EtOAc 5:1, #9–14 cyclohexane/EtOAc 2:1, product in #12–14). The title compound (36.1 mg, 51 %) was obtained as a colorless solid. M.p. 82–84 °C.

Method C: At 0 °C P_4O_{10} (12.62 g, 44.45 mmol, 1.2 equiv) was added to a solution of dibromolevulinic acid (**8**; 10.15 g, 37.04 mmol) in CH_2Cl_2 (150 mL). After 30 min, the solution was allowed to reach room temperature and heated at reflux for 1.5 h. After cooling to room temperature, it was filtered and concentrated in vacuo. A solution of the intermediate (8.094 g) in CH_2Cl_2 (75 mL) was cooled to 0 °C, and NEt_3 (5.29 mL, 3.84 g, 38.0 mmol, 1.03 equiv for **8**) was added. After 1 h, the mixture was first warmed to room temperature and then heated at reflux for 1 h. Aq. NH_4Cl (40 mL) was added, and the mixture extracted with (6 × 20 mL). The combined organic extracts were dried with Na_2SO_4. Evaporation in vacuo afforded a residue which was submitted to flash chromatography (5 cm, cyclohexane/EtOAc 20:1, #8–17 cyclohexane/EtOAc 10:1, #18–36 cyclohexane/EtOAc 2:1, product in #21–36) to afford the title compound (3.544 g, 55 % with respect to **8**) as a slightly yellow solid. M.p. 82–84 °C; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.11$ (s, 1′-H), 6.32 (d, $J_{3,4} = 5.6$, 3-H), 7.38 (d, $J_{4,3} = 5.6$, 4-H); the *Z*-configuration of the exocyclic double bond was proved by the NOE observed at 4-H ($\delta = 7.38$) while irradiating 1′-H ($\delta = 6.11$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 92.41$ (C-1′)*, 120.76 (C-3)*, 141.72 (C-4)*, 152.41 (C-5), 168.23 (C-2); *distinguishable by a C,H-correlation spectrum; IR ($CDCl_3$): $\tilde{\nu} = 3075$, 1780, 1750, 1725, 1640, 1555, 1170, 1110, 1075, 935, 885, 820, 780, 730 cm^{-1}; elemental analysis calcd (%) for $C_5H_3BrO_2$ (174.4): C 34.32, H 1.73; found: C 34.20, H 1.61.

3,5-Dibromolevulinic acid (8):[13] A solution of Br_2 (35.64 g, 0.2230 mol, 2.1 equiv) in CH_2Cl_2 (20 mL) was added dropwise to a solution of levulinic acid (**7**; 12.32 g, 0.1062 mol) and 20 drops of HBr (45 % in H_2O) in CH_2Cl_2 (100 mL) at 0 °C. After stirring at room temperature for 2 h, the mixture was washed with H_2O (50 mL) and with aq. $Na_2S_2O_3$ (50 mL). The aq. phase was extracted with CH_2Cl_2 (4 × 20 mL). The combined organic extracts were dried with Na_2SO_4. Petroleum ether (60–80 °C) was added under vigorous stirring. The resulting precipitate was filtered off and the title compound (18.28 g, 63 %; ref.:[13] 40 %) obtained as colorless crystals. M.p. 110–111 °C; ref.:[13] 112–114 °C.

5-Bromolevulinic acid methyl ester (9):[16] At 70 °C a solution of Br_2 (11.80 g, 73.84 mmol, 1.0 equiv) in MeOH (20 mL) was added dropwise to a solution of levulinic acid (**7**; 8.60 g, 74.1 mmol) in MeOH (90 mL). The mixture was heated at reflux for 2 h and cooled to room temperature HBr was driven out with a stream of N_2 (for 30 min). The solution was washed with aq. $NaHCO_3$ (40 mL) and the aq. phase extracted with CH_2Cl_2 (4 × 20 mL). The combined organic phases were dried with Na_2SO_4 and evaporated in vacuo. Flash chromatography (6.0 cm, cyclohexane/EtOAc 20:1, #5–15 cyclohexane/EtOAc 15:1, #16–31 cyclohexane/EtOAc 10:1, #32–55 cyclohexane/EtOAc 5:1, product in #24–55) afforded the title compound (5.82 g, 38 %; ref.:[16] 30 %) as a colorless oil.

5-(Dibromomethylene)-2(5*H*)-furanone (10):[12,13] Dibromolevulinic acid **8** (4.77 g, 17.4 mmol) was treated with a mixture of oleum (18 mL, 65 % SO_3) and conc. H_2SO_4 (9 mL). The solution was stirred at 50–60 °C for 6 min and poured onto ice. The mixture was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic phases were dried with Na_2SO_4. The solvent was evaporated in vacuo to afford a residue which was submitted to flash chromatography (5 cm, cyclohexane/EtOAc 15:1, #8–17 cyclohexane/EtOAc 10:1, #18–25 cyclohexane/EtOAc 5:1; #11–25) to afford the title compound (1.22 g, 28 %; ref.:[13] 8 %; ref.[12] 43 %) as a slightly yellow solid. M.p. 132–134 °C; ref.:[12] no details; ref.:[13] 137 °C.

3-(Trimethylsilyl)-2-propyn-1-ol (12):[19] At −78 °C BuLi (1.4 M in hexane, 31.4 mL, 44.0 mmol, 2.2 equiv) was added to a solution of propargyl alcohol (**11**; 1.12 g, 20.0 mmol) in THF (100 mL). After stirring for 30 min at this temperature Me_3SiCl (4.89 g, 45.0 mmol, 2.2 equiv) was added. The solution was warmed to room temperature and HCl (2 M, 50 mL) was added. After stirring for 1 h the aq. phase was extracted with *t*BuOMe (100 mL). The combined organic phases were washed with aq. $NaHCO_3$ (100 mL) and brine (100 mL). The organic phase was dried with $MgSO_4$ and the solvent evaporated in vacuo to afford an oily residue. The title compound (1.855 g, 72 %; ref.:[19] 82 %) was obtained after distillation as a colorless oil (b.p. 69–72 °C, 10 mbar; ref.:[19] 95–96 °C, 22 Torr).

3-(Trimethylsilyl)-2-propynal (13):[21] Alcohol **12** (11.90 g, 92.83 mmol) was added dropwise at 0 °C within 10 min to a suspension of PCC (32.56 g, 0.151 mol; 50 % on silica gel, 1.63 equiv) in CH_2Cl_2 (300 mL). After 2 h the dark suspension was filtered twice through a pad of silica gel and washed with CH_2Cl_2 (40 mL). The solvent was evaporated in vacuo to afford an oily residue. The title compound (8.90 g, 76 %; ref.:[21] 65 %) was obtained after distillation as a slightly yellow oil (b.p. 44 °C, 20 mbar; ref.:[21] 52–57 °C, 30 Torr).

1-(Trimethylsilyl)-1,5-hexadiyn-3-ol (14):[22] At 0 °C propargyl bromide (80 % in toluene, 5.340 g, 44.9 mmol, >1.0 equiv) was added within 30 min to a suspension of Mg (1.638 g, 67.4 mmol, >1.5 equiv) and $HgCl_2$ (220 mg, 0.812 mmol, 2 mol %) in Et_2O (50 mL). After stirring for 1 h at this temperature, this solution was added at −78 °C within 15 min to a solution of propargyl aldehyde **13** (5.650 g, <44.9 mmol) in Et_2O (50 mL). After stirring for 15 min 0 °C and 30 min at room temperature, the reaction was terminated by addition of aq. NH_4Cl (45 mL) and H_2O (50 mL). The aq. phase was extracted with Et_2O (3×50 mL). The combined organic phases were dried with Na_2SO_4. The solvent was evaporated in vacuo to afford the crude product [7.420 g, contaminated with 24 mol % = 13 wt % Et_2O and a little amount of toluene; the yield of **14** was therefore 6.479 g (87 %; ref.:[22] 89 %)].

Novel preparation of 1,5-hexadiyn-3-ol (15):[24] Silylalkyne **14** (6.479 g, 39.10 mmol) was added to a solution of K_2CO_3 (5.470 g, 39.10 mmol, 1.0 equiv) in MeOH (90 mL). After 24 h the reaction was terminated by addition of aq. NH_4Cl (50 mL) and H_2O (20 mL). The aq. phase was extracted with Et_2O (4×60 mL) and the combined organic extracts were washed with brine. After drying with Na_2SO_4 the solvent was evaporated in vacuo to afford the title compound (2.898 g, 78 %) as a slightly yellow, unpleasantly smelling oil.

(*Z*)-5-[*trans*,*trans*-4-Hydroxy-7-(tributylstannyl)-2,6-heptadienylidene]-2(5*H*)-furanone (16) and (*Z*)-5-[*trans*,*trans*-5-hydroxy-7-(tributylstannyl)-2,6-heptadienylidene]-2(5*H*)-furanone (*iso*-16) as a 47:53 mixture: A degassed solution of bromide **6** (152.3 mg, 0.874 mmol) in THF (2 mL) was added within 20 min to a degassed solution of bis(stannane) **5** (1.182 g, 1.751 mmol, 2.00 equiv), $[Pd(dba)_2]$ (20.1 mg, 0.0348 mmol, 0.04 equiv), and $AsPh_3$ (42.3 mg, 0.137 mmol, 0.15 equiv) in THF (6 mL). After 1 h the solvent was evaporated in vacuo and the resulting residue purified by flash chromatography (2.5 cm, cyclohexane/EtOAc/NEt_3 40:4:1, #9–14 cyclohexane/EtOAc/NEt_3 40:10:1, #15–23 cyclohexane/EtOAc/NEt_3 20:10:1, product in #17–24). The title compounds (233.1 mg, 55 %) were obtained as an inseparable 47:53 mixture [calculated from ^{1}H NMR integrals of 4′-H_{16} (δ = 4.34) and 5′-$H_{iso\text{-}16}$ (δ = 4.21) resp. 2′-H_{16} (δ = 6.79) and 2′-$H_{iso\text{-}16}$ (δ = 6.67)] as yellow oils, which rapidly turned brown. ^{1}H NMR (500 MHz, $CDCl_3$; assignment by comparison with the ^{1}H NMR spectrum of regioisomerically pure **16**): δ = 0.74–0.97 (m, 3×Sn$CH_2CH_2CH_2CH_3$ each by **16** and *iso*-**16**), 1.30 (tq, both J_{vic} = 7.4, 3×Sn $CH_2CH_2CH_2CH_3$ each by **16** and *iso*-**16**), 1.41–1.56 (m, 3×Sn$CH_2CH_2CH_2CH_3$ each by **16** and *iso*-**16**), 1.66 [d, $J_{OH,5'}$ = 4.3, OH (*iso*-**16**)], 1.86 [d, $J_{OH,4'}$ = 4.0, OH (**16**)], 2.36–2.54 [m, 5′-H_2 (**16**), 4′-H_2 (*iso*-**16**)], 4.21 [m, 5′-H (*iso*-**16**)], 4.34 [m, 4′-H (**16**)], 5.80 [d, $J_{1',2'}$ = 11.2, 1′-H (*iso*-**16**)], 5.81 [d, $J_{1',2'}$ = 11.2, 1′-H (**16**)], 5.93 [ddd, $J_{6',7'}$ = 18.9, $J_{6',5'\text{-}H(1)}$ = 6.9, $J_{6',5'\text{-}H(2)}$ = 6.3, 6′-H (**16**)], 5.97–6.21 [m, 3-H (**16** and *iso*-**16**), 3′-H (**16** and *iso*-**16**), 6′-H (*iso*-**16**), 7′-H (*iso*-**16**)], superimposes 6.10 [d, $J_{7',6'}$ = 18.9, $^4J_{7',5'\text{-}H(1)}$ = $^4J_{7',5'\text{-}H(2)}$ = 1.2, 7′-H (**16**)], 6.67 [ddt, $J_{2',3'}$ = 15.4, $J_{2',1'}$ = 11.2, $^4J_{2',4'\text{-}H(1)}$ = $^4J_{2',4'\text{-}H(2)}$ = 1.4, 2′-H (*iso*-**16**)], 6.79 [dd, $J_{2',3'}$ = 15.5, $J_{2',1'}$ = 11.3, J_{allyl} = 1.4 Hz, 2′-H (**16**)], 7.35 [d, $J_{4,3}$ = 5.4, 4-H (*iso*-**16**)], 7.37 [d, $J_{4,3}$ = 5.2, 4-H (**16**)]; IR (film): $\tilde{\nu}$ = 3425, 2955, 2925, 2870, 2855, 1780, 1750, 1645, 1545, 1465, 1375, 1335, 1110, 1065, 1045, 1025, 990, 975, 935, 880, 805, 670 cm^{-1}; elemental analysis calcd (%) for $C_{23}H_{38}O_3Sn$ (480.2): C 57.40, H 7.96; found: C 57.57, H 8.00.

***trans*-3-(Tributylstannyl)-2-propen-1-ol (17)**:[26] At −78 °C BuLi (1.45 M in Hexan, 44.0 mL, 63.8 mmol, 2.23 equiv) was added within 1.5 h to a suspension of CuCN (2.720 g, 30.37 mmol, 1.09 equiv) in THF (100 mL). After warming to room temperature, the solution was immediately cooled to −78 °C again. Freshly distilled Bu_3SnH (17.67 g, 60.74 mmol, 2.18 equiv) was added within 15 min, followed by addition of freshly distilled propargyl alcohol (**11**; 1.56 g, 27.86 mmol). After 45 min, the solution was warmed to −10 °C, diluted with *t*BuOMe (50 mL) and poured onto aq. NH_3-Lsg. (2.5 %, 100 mL). The aq. phase was extracted with *t*BuOMe (5×50 mL), and the combined organic phases dried with Na_2SO_4. The solvent was evaporated in vacuo to afford an oily residue which was purified by flash chromatography (5 cm, cyclohexane/EtOAc/NEt_3 150:5:3, #17–52 cyclohexane/EtOAc/NEt_3 100:10:3, #53–58 cyclohexane/EtOAc/NEt_3 50:5:1, product in #32–58) to afford the title compound (8.227 g, 79 %; ref.:[26] 52 %) as a slightly yellow oil.

***trans*-3-(Tributylstannyl)-2-propen-1-al (18)**:[28] At 0 °C Dess–Martin periodinane (3.237 g, 7.632 mmol, 1.30 equiv) was added to a solution of alcohol **17** (2.038 g, 5.871 mmol) in CH_2Cl_2 (15 mL). The solution was allowed to warm to room temperature within 2.5 h. After evaporation of the solvent in vacuo the resulting residue was purified by flash chromatography (4.5 cm, cyclohexane/EtOAc/NEt_3 100:10:3, product in #2–7) to afford the title compound (1.889 g, 93 %) as a yellow oil.

***trans*-1-(Tributylstannyl)-1-hexen-5-yn-3-ol (20)**: At 0 °C propargyl bromide (80 % in toluene, 278 mg, 1.87 mmol, 1.0 equiv) was added dropwise to a suspension of Mg (69.1 mg, 2.88 mmol, 1.54 equiv) and $HgCl_2$ (14.9 mg, 5.49 μmol, 0.003 equiv) in Et_2O (5 mL). After 30 min the solution was warmed to room temperature, and immediately cooled to 0 °C again. The solution was added dropwise at 0 °C to a solution of aldehyde **18** (641.8 mg, 1.86 mmol) in Et_2O (5 mL). After 45 min the reaction was terminated by addition of phosphate buffer (pH 7.2, 10 mL). The aq. phase was extracted with *t*BuOMe (5×10 mL) and the combined organic phases were dried with Na_2SO_4. Evaporation of the solvent afforded an oily residue which was purified by flash chromatography (3 cm, cyclohexane/EtOAc/NEt_3 250:10:6, #13–19 cyclohexane/EtOAc/NEt_3 150:10:6, product in #12–19) to afford the title compound (483.8 mg, 68 %) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.83–0.97 (m, 3×Sn$CH_2CH_2CH_2CH_3$), superimposes 0.89 (t, J_{vic} = 7.3, 3×Sn$CH_2CH_2CH_2CH_3$), 1.31 (tq, both J_{vic} = 7.3, 3×Sn$CH_2CH_2CH_2CH_3$), 1.42–1.57 (m, 3×Sn$CH_2CH_2CH_2CH_3$), 2.00 (br. d, $J_{OH,3}$ = 4.8, OH), 2.04 (t, $^4J_{6,4}$ = 2.7, 6-H), AB signal (δ_A = 2.44, δ_B = 2.49, J_{AB} = 16.7, in addition split by $J_{A,3}$ = 6.6, $^4J_{A,6}$ = 2.7, $J_{B,3}$ = 5.3, $^4J_{B,6}$ = 2.7, 4-H_2), 4.26 (m, 3-H), 6.06 (dd, $J_{2,1}$ = 19.1, $J_{2,3}$ = 5.1, each peak flanked by Sn isotope satellites as 2 interlocked d, $^3J_{2,^{119}Sn}$ = 62.9, $^3J_{2,^{117}Sn}$ = 60.1, 2-H), 6.26 (dd, $J_{1,2}$ = 19.2, $J_{1,3}$ = 1.3, each peak flanked by Sn isotope satellites as 2 d, $^2J_{^{119}Sn}$ = 68.9 $^2J_{^{117}Sn}$ = 65.5, 1-H); ^{13}C NMR (125 MHz, $CDCl_3$; peaks of contaminant at 70.72 and 148.21): δ = 9.49 (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1'}$ = 345.5, $^1J_{^{117}Sn,C\text{-}1'}$ = 330.6, 3×Sn$CH_2CH_2CH_2CH_3$), 13.68 (3×Sn$CH_2CH_2CH_2CH_3$), 27.24 (3×Sn$CH_2CH_2CH_2CH_3$), 27.39 (C-4), 29.03 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2'}$ = $^2J_{^{117}Sn,C\text{-}2'}$ = 20.3, 3×Sn$CH_2CH_2CH_2CH_3$), 70.67 (C-6)*, 72.80 (C-3)*, 80.48 (C-5), 129.53 (C-1)**, 148.23 (C-2)**; *,**distinguishable by a C,H correlation spectrum; IR (film): $\tilde{\nu}$ = 3315, 2955, 2925, 2870, 2850, 1460, 1375, 1075, 1035, 990, 865, 690, 640, 595 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{34}OSn$ (386.2): C 56.13, H 8.90; found: C 56.16, H 8.97.

(*Z*)-5-(*trans*-4-Hydroxy-2-hepten-6-ynylidene)-2(5*H*)-furanone (21): Stannane **20** (238 mg, 0.618 mmol, 1.10 equiv) was added to a solution of bromide **6** (97.5 mg, 0.561 mmol), $[Pd(dba)_2]$ (16.2 mg, 28.2 mmol, 0.05 equiv), and $AsPh_3$ (24.2 mg, 79.1 mmol, 0.14 equiv) in THF (4 mL). After 3 h the solvent was evaporated in vacuo to afford an oily residue which was purified by flash chromatography (2.5 cm, cyclohexane/EtOAc/NEt_3 150:30:6, #11–16 cyclohexane/EtOAc/NEt_3 100:50:5, #17–28 cyclohexane/EtOAc/NEt_3 100:100:6, product in #21–28) to afford the title compound (81.6 mg contaminated with 9.6 mol % = 4.7 wt % *t*BuOMe, hence 77.8 mg pure **21**, 73 %), as a yellow, instable oil. It was directly used in the next reaction without acquiring IR spectrum or elemental analysis; ^{1}H NMR (500 MHz, $CDCl_3$; contains 9.6 mol % *t*BuOMe): δ = 2.10 (t, $^4J_{7',5'}$ = 2.6, 7′-H), 2.50–2.54 (assignment by the integral: OH), completely superimposed by AB signal (δ_A = 2.52, δ_B = 2.54, J_{AB} = 16.7, in addition split by $J_{A,4'}$ = 6.2, $^4J_{A,7'}$ = 2.6, $J_{B,4'}$ = 5.9, $^4J_{B,7'}$ = 2.6, 5′-H_2), 4.46 (very br. ddd, $J_{4',5'\text{-}H(A)} \approx J_{4',5'\text{-}H(B)} \approx J_{4',3'} \approx$ 5.8, 4′-H), 5.85 (d, $J_{1',2'}$ = 11.2, 1′-H), 6.12 (ddd, $J_{3',2'}$ = 15.3, $J_{3',4'}$ = 5.8, $^4J_{3',1'}$ = 0.6, 3′-H), 6.20 (d, $J_{3,4}$ = 5.4, 3-H), 6.84 (ddd, $J_{2',3'}$ = 15.5, $J_{2',1'}$ = 11.4, $^4J_{2',4'}$ = 1.4, 2′-H), 7.41 (d, $J_{4,3}$ = 5.4, 4-H); ^{13}C NMR (125 MHz, $CDCl_3$; contains 9.6 mol % *t*BuOMe): δ = 27.33 (C-5′)*, 70.02 (C-4′)*, 71.34 (C-7′)*, 79.66 (C-6′), 113.36 (C-1′)**, 119.45 (C-3)***, 123.73 (C-2′)**, 140.25 (C-3′)**, 143.23 (C-4)***, 149.12 (C-5), 169.40 (C-2); *, **, ***distinguishable by a C,H correlation spectrum.

(*Z*)-5-[*trans*,*trans*-4-Hydroxy-7-(tributylstannyl)-2,6-heptadienylidene]-2(5*H*)-furanone (16) and (*Z*)-5-[*trans*-4-hydroxy-6-(tributylstannyl)-2,6-heptadienylidene]-2(5*H*)-furanone (22): Bu_3SnH (83.0 mg, 0.285 mmol, 1.20 equiv) was added to a degassed solution of alkyne **21** (45.0 mg, 0.238 mmol) and $[PdCl_2(PPh_3)_2]$ (3.4 mg, 48 μmol, 0.02 equiv) in THF (2 mL). After 30 min the solvent was evaporated in vacuo to afford an oily residue which was purified by flash chromatography (2.5 cm, cyclo-

hexane/EtOAc/NEt_3 200:20:6, #17–27 cyclohexane/EtOAc/NEt_3 200:30:6, #28–45 cyclohexane/EtOAc/NEt_3 200:40:6). Fractions #21–27 contained **22** (42.0 mg, 37%) and fractions #36–45 contained **16** (41.3 mg, 36%) as yellow oils, which rapidly turned brown. Analytic data for **16**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.80$–0.95 (m, $3\times SnCH_2CH_2CH_2CH_3$), superimposes 0.88 (t, $J_{vic} = 7.4$, $3\times SnCH_2CH_2CH_2CH_3$), 1.30 (tq, both $J_{vic} = 7.4$, $3\times SnCH_2CH_2CH_2CH_3$), 1.40–1.57 (m, $3\times SnCH_2CH_2CH_2CH_3$), 1.83 (d, $J_{OH,4'} = 3.7$, OH), AB signal, which is not completely resolved in the A part ($\delta_A = 2.39$, $\delta_B = 2.50$, $J_{AB} = 13.9$, in addition split by $J_{A,4'} = J_{A,6'} = 7.1$, $^4J_{A,7'} = 1.0$, $J_{B,6'} = 6.2$, $J_{B,4'} = 5.0$, $^4J_{B,7'} = 1.3$, 5′-H_2), 4.34 (m, 4′-H), 5.81 (d, $J_{1',2'} = 11.2$, 1′-H), 5.93 (ddd, $J_{6',7'} = 18.8$, $J_{6',5'\text{-H(A)}} = 6.9$, $J_{6',5'\text{-H(B)}} = 6.2$, 6′-H), 6.06 (ddd, $J_{3',2'} = 15.4$, $J_{3',4'} = 5.8$, $^4J_{3',1'} = 0.7$, 3′-H), one peak superimposed by 6.11 (dt, $J_{7',6'} = 18.9$, $^4J_{7',5'\text{-H(A)}} = {}^4J_{7',5'\text{-H(B)}} = 1.2$, 7′-H), 6.18 (d, $J_{3,4} = 5.4$, 3-H)*, 6.79 (ddd, $J_{2',3'} = 15.5$, $J_{2',1'} = 11.3$, $J_{allyl} = 1.4$, 2′-H), 7.37 (d, $J_{4,3} = 5.2$, 4-H); elemental analysis calcd (%) for $C_{23}H_{38}O_3Sn$ (480.2): C 57.40, H 7.96; found: C 57.44, H 8.12.

Analytic data for **22**: ^{1}H NMR (500 MHz, $CDCl_3$; peak of contaminant at $\delta = 5.80$): $\delta = 0.87$–1.01 (m, $3\times SnCH_2CH_2CH_2CH_3$), superimposes 0.90 (t, $J_{vic} = 7.3$, $3\times SnCH_2CH_2CH_2CH_3$), 1.32 (tq, both $J_{vic} = 7.3$, $3\times SnCH_2CH_2CH_2CH_3$), 1.44–1.56 (m, $3\times SnCH_2CH_2CH_2CH_3$), 1.89 (d, $J_{OH,4'} = 2.8$, OH), AB signal ($\delta_A = 2.41$, $\delta_B = 2.59$, $J_{AB} = 13.7$, in addition split by $J_{A,4'} = 9.2$, flanked by Sn isotope satellites as 1 incompletely resolved d, $^3J_{A,^{119}Sn} \approx {}^3J_{A,^{117}Sn} \approx 60$, $J_{B,4'} = 4.0$, flanked by Sn isotope satellites as 1 incompletely resolved dm, $^3J_{B,^{119}Sn} \approx {}^3J_{B,^{117}Sn} \approx 17$, 5′-$H_2$), 4.24 (m, 4′-H), 5.36 [d, $J_{gem} = 2.6$, each peak flanked by Sn isotope satellites as 2 interlocked d, $^3J_{7'\text{-H}(Z),^{119}Sn} = 60.6$, $^3J_{7'\text{-H}(Z),^{117}Sn} = 58.1$, 7′-H($Z$)]*, 5.82 (d, $J_{1',2'} = 11.4$, 1′-H), low-field peak is exactly on middle peak of 5.81 [ddd, $^2J_{gem} = {}^4J_{7'\text{-H}(E),5'\text{-H(A)}} = {}^4J_{7'\text{-H}(E),5'\text{-H(B)}} = 1.7$, each peak flanked by Sn isotope satellites as 2 d, $^3J_{7'\text{-H}(E),^{119}Sn} = 132.7$, $^3J_{7'\text{-H}(E),^{117}Sn} = 127.4$, 1′-H, 7′-H($E$)]*, 6.06 (ddd, $J_{3',2'} = 15.5$, $J_{3',4'} = 6.0$, $^4J_{3',1'} = 0.7$, 3′-H), 6.18 (d, $J_{3,4} = 5.00$, 3-H), 6.80 (ddd, $J_{2',3'} = 15.5$, $J_{2',1'} = 11.3$, $J_{allyl} = 1.4$, 2′-H), 7.37 (d, $J_{4,3} = 5.4$, 4-H); *distinguishable by comparison with the $^3J_{Sn,H}$ coupling constants of vinylstannans: $^3J_{H(Z),Sn} = 50$–75 Hz and $^3J_{H(E),Sn} = 100$–150 Hz;[59] elemental analysis calcd (%) for $C_{23}H_{38}O_3Sn$ (480.2): C 57.40, H 7.96; found: C 57.34, H 8.13.

1,4-Dichloro-2-butyne (23):[3]

***trans*-2-Heptene-4,6-diyn-1-ol (25)**:[30] Li (6.80 g, 1.00 mol, 6.0 equiv) and a catalytic amount of $Fe(NO_3)_2\cdot 9H_2O$ were dissolved in liquid NH_3 (1000 mL). After stirring at −45 °C for 1 h 1,4-dichloro-2-butyne (**23**; 40.96 g, 333 mmol, 2.0 equiv) was added within 75 min. After 15 min epichlorohydrin (**24**; 15.42 mg, 0.1667 mol) was added within 40 min at the same temperature. After 3.5 h NH_4Cl (18 g) was added and the NH_3 was allowed to evaporate overnight. H_2O (400 mL) was added and the aq. phase extracted with *t*BuOMe (5×200 mL). The combined organic phases were dried with $MgSO_4$ and the solvent evaporated in vacuo. The residue was purified by flash chromatography {5 cm, Al_2O_3 B [desactivated with 10 vol.% HOAc (1.6 M)], cyclohexane, #20–39 cyclohexane/EtOAc 3:1, #40–49 cyclohexane/EtOAc 1:1, product in #32–49} to afford the title compound [2.943 g, 17%, contaminated with 1.472 g EtOAc (40 mol% = 33 wt%); ref.:[30] 21%] as a brown solid. Further removal of the solvent led to complete decomposition of the product.

***trans*-1-(*tert*-Butyldimethylsiloxy)-2-heptene-4,6-diyne (26)**: At 0 °C *t*BuMe$_2$SiCl (50 wt% in toluene, 1.215 g, 8.10 mmol, 1.0 equiv) was added to a solution of heptendiynol **25** (849 mg, 8.09 mmol) and imidazole (1.099 g, 16.17 mmol, 2.0 equiv) in CH_2Cl_2 (20 mL). After 2 h the solution was poured on H_2O (50 mL) and the aq. phase extracted with CH_2Cl_2 (2×20 mL). The solvent was evaporated in vacuo and the residue purified by flash chromatography (2 cm, cyclohexane/EtOAc 30:1, product in #5–19) to afford the title compound (1.328 g, 75%) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.07$ [s, $Si(CH_3)_2$], 0.91 [s, $C(CH_3)_3$], 2.40 (s, 7-H), 4.25 (dd, $J_{1,2} = 3.8$, $^4J_{1,3} = 2.3$, 1-H_2), 5.80 (dm, $J_{3,2} \approx 15.7$, 3-H), 6.43 (dt, $J_{2,3} = 15.8$, $J_{2,1} = 3.9$, 6-H); IR ($CDCl_3$): $\tilde{\nu} = 3305$, 2955, 2930, 2885, 2860, 2205, 1255, 1195, 1135, 1065, 1010, 835 cm^{-1}; elemental analysis calcd (%) for $C_{13}H_{20}OSi$ (221.1): C 70.85, H 9.15; found: C 70.62, H 8.89.

***trans*-1-(*tert*-Butyldimethylsiloxy)-7-iodo-2-heptene-4,6-diyne (27)**: At −78 °C BuLi (1.4 M in hexane, 1.2 mL, 1.7 mmol, 1.2 equiv) was added to a solution of enediyne **26** (300 mg, 1.37 mmol) in THF (10 mL). After 5 min I_2 (423 mg, 1.64 mmol, 1.2 equiv) was added. After 25 min the cooling bath was removed and the solution stirred for another 15 min. The solvent was evaporated in vacuo and the residue purified by flash chromatography (2 cm, cyclohexane, #5–18 cyclohexane/EtOAc 10:1, product in #10–18) to afford the title compound (416 mg, 87%) as a brown solid. M.p. 36 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.06$ [s, $Si(CH_3)_2$], 0.91 [s, $C(CH_3)_3$], 4.26 (dd, $J_{1,2} = 3.9$, $^4J_{1,3} = 2.3$, 1-H_2), 5.84 (dt, $J_{3,2} = 15.7$, $^4J_{3,1} = 2.3$, 3-H), 6.40 (dt, $J_{2,3} = 15.7$, $J_{2,1} = 3.9$, 2-H); IR ($CDCl_3$): $\tilde{\nu} = 2955$, 2930, 2055, 1730, 1255, 1135, 1065, 1010, 835 cm^{-1}; elemental analysis calcd (%) for $C_{13}H_{19}IOSi$ (346.0): C 45.09, H 5.53; found: C 45.47, H 5.71.

***Z*-5-[all-*trans*-14-(*tert*-Butyldimethylsiloxy)-4-hydroxy-2,6,12-tetradecatriene-8,10-diynylidene]-2(5*H*)-furanone (28) as a 50:50 mixture with the 5-hydroxy isomer (*iso*-28)**: A mixture of $[Pd(dba)_2]$ (3.3 mg, 5.8 μmol, 0.05 equiv) and $AsPh_3$ (7.0 mg, 23 μmol, 0.2 equiv) was added to a solution of diyne **27** (60 mg, 0.17 mmol, 1.5 equiv) and a 53:47 mixture of the stannanes **16** and *iso*-**16** (54.0 mg, 0.115 mmol) in THF (3 mL). After 24 h the solvent was evaporated in vacuo and the residue purified by flash chromatography (2 cm, cyclohexane/EtOAc 3:1, #11–18 cyclohexane/EtOAc 1:1, product in #16–18) to afford the title compounds as an inseparable 50:50 mixture (24.0 mg, 51%) as yellow oils; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.07$ [s, $Si(CH_3)_2$], 0.91 (s, $C(CH_3)_3$], 2.42–2.57 [m, 5′-H_2 (**28**), 4′-H_2 (*iso*-**28**)], 4.25 (incompletely resolved dd, $J_{14',13'} = 3.7$, $^4J_{14',12'} = 1.8$, 14′-H_2), 4.31–4.45 [m, 4′-H (**28**), 5′-H (*iso*-**28**)], 5.78–5.90 and 5.96–6.42 (2 m à 2 H bzw. 5 H; 3-H, 1′-H, 3′-H, 6′-H, 7′-H, 12′-H, 13′-H), 6.68 [dd, $J_{2',3'} = 15.5$, $J_{2',1'} = 11.3$, 2′-H (**28**)], 6.79 [incompletely resolved ddt, $J_{2',3'} \approx 15.5$, $J_{2',1'} \approx 11.3$, $^4J_{2',4'} \approx 1.1$, 2′-H (*iso*-**28**)], 7.37 [d, $J_{4,3} = 5.2$, 4-H (**28**)*], partly superimposed by 7.38 [d, $J_{4,3} = 4.7$, 4-H (*iso*-**28**)*]; *interchangeable; IR ($CDCl_3$): $\tilde{\nu} = 2945$, 2860, 1750, 1545, 1415, 1335, 1260, 1185, 1135, 1045, 975, 830 cm^{-1}; (m/z) = 353.12091 ± 5 mDa [M^+], confirmed by HRMS (EI, 70 eV).

***Z*-5-[all-*trans*-14-(*tert*-Butyldimethylsiloxy)-2,4,6,12-tetradecatetraene-8,10-diynylidene]-2(5*H*)-furanone (*trans*-29)**: At −78 °C Tf_2O (24.7 mg, 87.8 μmol, 1.5 equiv) was added to a 50:50 mixture of the alcohols **28** and *iso*-**28** (24.0 mg, 58.5 μmol) and NEt_3 (29.5 mg, 293 μmol, 5.0 equiv) in CH_2Cl_2 (5 mL). After 25 min the solution was allowed to warm to −20 °C within 2 h. The solution was directly submitted to flash chromatography (2 cm, cyclohexane/EtOAc 3:1). Fractions #4–9 contained 9.0 mg of severely contaminated product(s) making a structural assignment impossible. Fractions #10–15 contained the title compound *trans*-**29** (11.0 mg, 48%) as a yellow solid. ^{1}H NMR [500 MHz, $CDCl_3$; contains some contaminant(s)]: $\delta = 0.07$ [s, $Si(CH_3)_2$], 0.91 (s, $C(CH_3)_3$], 4.27 (dd, $J_{14',13'} = 3.8$, $^4J_{14',12'} = 2.4$, 14′-H_2), 5.77 (d, $J_{7',6'} = 15.4$, 7′-H), 5.89 (d, $J_{1',2'} = 11.8$, 1′-H; completely superimposes and therefore only visible by the integral: $J_{12',13'}$ presumably up to 16 Hz, 12′-H), 6.18 (d, $J_{3,4} = 5.4$, 3-H), 6.39 (dt, $J_{13',12'} = 15.7$, $J_{13',14'} = 4.0$, 13′-H), 6.41–6.55 (m, 3′-H, 4′-H, 5′-H,), 6.78 (dd, $J_{6',7'} = 15.2$, $J_{6',5'} = 10.1$, 6′-H), partly interlocked with 6.83 (dd, $J_{2',3'} = 13.9$, $J_{2',1'} = 11.8$, 2′-H), 7.37 (d, $J_{4,3} = 5.2$, 4-H); the H,H-correlation spectrum confirms the assignment by the following cross-peaks: 1) 14′-H_2 ($\delta = 4.27$) ⇔ 13′-H ($\delta = 6.39$) ⇔ 12′-H ($\delta = 5.89$); 2) 7′-H ($\delta = 5.77$) ⇔ 6′-H ($\delta = 6.78$) ⇔ amongst others 5′-H ($\delta = 6.41$–6.55, together with 3′-H and 4′-H); 3) 1′-H ($\delta = 5.89$) ⇔ 2′-H ($\delta = 6.83$) ⇔ 3′-H ($\delta = 6.41$–6.55, together with 4′-H and 5′-H); 4) 3-H ($\delta = 6.18$) ⇔ 4-H ($\delta = 7.37$); IR ($CDCl_3$): $\tilde{\nu} = 2930$, 2875, 1775, 1750, 1530, 1445, 1415, 1330, 1260, 1120, 1065, 1045, 835 cm^{-1}; (m/z) = 392.18077 ± 5 mDa [M^+] confirmed by HRMS (EI, 70 eV).

***Z*-5-(all-*trans*-14-Hydroxy-2,4,6,12-tetradecatetraene-8,10-diynylidene)-2(5*H*)-furanone (30)**: At 0 °C HF/pyridine complex (50 μL, 1.2 mmol, 44.7 equiv) was added to silyl ether *trans*-**29** (10.5 mg, 26.8 μmol) in THF (5 mL). After 2 h 15 min more HF/pyridine complex (100 μL, 2.4 mmol, 89.6 equiv) was added. Silica gel (ca. 200 mg) was added after 2 h 45 min and the mixture stirred at 0 °C for 15 min. After filtration through a pad of Celite, the solvent was evaporated in vacuo and the residue purified by flash chromatography (2 cm, cyclohexane/EtOAc 3:1, #10–21 cyclohexane/EtOAc 1:3, product in #16–21) affording an orange solid (5.0 mg). It contained aliphatic impurities, therefore the yield of the title compound is < 67%; ^{1}H NMR (300 MHz, $CDCl_3$; contains insoluble material): $\delta = 4.27$ (dd, $J_{14',13'} = 4.6$, $^4J_{14',12'} = 1.8$, 14′-H_2), 5.77 (d, $J_{7',6'} = 15.1$, 7′-H), 5.90 (d, $J_{1',2'} = 11.8$, 1′-H; completely superimposes and therefore only visible by the integral: $J_{12',13'}$ presumably up to 16 Hz, 12′-H), 6.19 (d, $J_{3,4} = 5.2$, 3-H), 6.37–6.58 (m, 3′-H, 4′-H, 5′-H, 13′-H), 6.73–6.90 (m, 2′-H,

6′-H), 7.37 (d, $J_{4,3}=5.4$, 4-H); signal assignment by comparison with the analogous resonances of precursor *trans*-**29**; the OH signal was not identified.

***Z*-5-(all-*trans*-14-Oxo-2,4,6,12-tetradecatetraene-8,10-diynylidene)-2(5*H*)-furanone (31)**: Dess–Martin periodinane (9.1 mg, 21 μmol, >1.2 equiv) was added to a solution of (impure) alcohol **30** (5.0 mg, ≤ 18 μmol) in CH_2Cl_2 (3 mL). After 1 h the mixture was directly submitted to flash chromatography (2 cm, cyclohexane/*t*BuOMe 3:1, #8–26 cyclohexane/*t*BuOMe 3:2, product in #20–26). The title compound (3.2 mg, >64%; 43% over two steps) was obtained as a red solid; ^{1}H NMR [500 MHz, $CDCl_3$, contains aliphatic signals (polymer?) and minor contaminants]: $\delta=5.81$ (d, $J_{7',6'}=15.5$, 7′-H), 5.90 (d, $J_{1',2'}=11.7$, 1′-H), 6.21 (d, $J_{3,4}=5.2$, 3-H), 6.43–6.58 (m, 3′-H, 4′-H, 5′-H, 13′-H), 6.69 (dd, $J_{12',13'}=15.9$, $^7J_{12',7'}=0.8$, 12′-H), 6.87 (dd, $J_{2',3'}=14.2$, $J_{2',1'}=11.4$, 2′-H), strongly interlocked with 6.88 (dd, $J_{6',7'}=15.4$, $J_{6',5'}=11.0$, 6′-H), 7.38 (d, $J_{4,3}=5.5$, 4-H), 9.60 (d, $J_{14',13'}=7.6$, 14′-H); the H,H-correlation spectrum confirms the assignment by the following cross-peaks: 1) 3-H ($\delta=6.21$) ⇔ 4-H ($\delta=7.38$); 2) 1′-H ($\delta=5.90$) ⇔ 2′-H ($\delta=6.87$) ⇔ 3′-H ($\delta=6.43$–6.58; together with 4′-H, 5′-H and 13′-H); 3) 7′-H ($\delta=5.81$) ⇔ 6′-H ($\delta=6.88$) ⇔ 5′-H ($\delta=6.43$–6.58; together with 3′-H, 4′-H and 13′-H); 4) 12′-H ($\delta=6.69$) ⇔ 13′-H ($\delta=6.43$–6.58; together with 3′-H, 4′-H and 5′-H) ⇔ 14′-H ($\delta=9.60$); (m/z) = 276.07865 ± 5 mDa [M^+] confirmed by HRMS (EI, 70 eV).

(*Z*)-5-[all-*trans*-7-(Tributylstannyl)-2,4,6-heptatrienylidene]-2(5*H*)-furanone (*trans*,*trans*,*trans*-32): *Method A*: At −78°C a solution of Tf_2O (246 μL, 412 mg, 1.46 mmol, 1.40 equiv) in CH_2Cl_2 (2 mL) was added within 5 min via a transfer cannula (cooled with dry ice) to a solution of alcohols **16**/*iso*-**16** (500.3 mg, 1.042 mmol) and NEt_3 (0.74 mL, 0.54 g, 5.32 mmol, 5.11 equiv) in CH_2Cl_2 (5 mL). The solution was allowed to warm to −20°C within 2.5 h and recooled immediately to −78°C. The solution was poured on a short chromatography column (silica gel, 2× 8 cm) and eluated with cyclohexane/EtOAc/NEt_3 200:20:5. After evaporation of the solvent in vacuo the residue was purified by flash chromatography (2.5 cm, cyclohexane/EtOAc/NEt_3 200:10:5, #12–22 cyclohexane/EtOAc/NEt_3 200:20:5, product in #16–22) to afford the title compound (198.2 mg, 41%) as a yellow oil.

Method B: Stannane *trans*,*cis*,*trans*-**35** (302.0 mg, 0.460 mmol, 1.0 equiv) was added to a degassed solution of bromide **6** (80.0 mg, 0.460 mmol), [Pd(dba)$_2$] (13.8 mg, 0.024 mmol, 0.05 equiv), $AsPh_3$ (27.8 mg, 0.091 mmol, 0.20 equiv), and CuI (8.7 mg, 0.046 mmol, 0.10 equiv) in THF (3 mL). The solution was stirred at 40°C for 2 h, the solvent evaporated in vacuo and the residue purified by flash chromatography (2.5 cm, cyclohexane/EtOAc/NEt_3 100:5:4, #14–33 cyclohexane/EtOAc/NEt_3 100:10:4, product in #23–33). The title compound (116.9 mg, 55%) was obtained as an orange oil.

Method C: At −78°C BuLi (2.17 M in hexane, 0.11 mL, 0.24 mmol, 1.3 equiv) was added slowly to a solution of stannane *trans*,*trans*,*trans*-**35** (156 mg, 0.238 mmol, 1.3 equiv) in THF (1.5 mL). After 25 min $ZnCl_2$ (1.5 M in THF, 0.16 mL, 0.24 mmol, 1.3 equiv) was added and the solution allowed to warm to −20°C. After 1.5 h it was transferred at 0°C within 4 min to a solution of bromide **6** (31.2 mg, 0.179 mmol) and [Pd(PPh$_3$)$_4$] (10.3 mg, 8.95 μmol, 0.05 equiv) in THF (1 mL). After 1 h at this temperature, the solution was concentrated in vacuo to half of its volume and filtered through a pad of Celite. The solvent was evaporated in vacuo and the residue purified by flash chromatography (2.5 cm, cyclohexane/EtOAc/NEt_3 200:20:2, #10–18 cyclohexane/EtOAc/NEt_3 200:40:2, product in #14–18) to afford the title compound (52.1 mg, 63%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.86$–1.00 (m, 3× SnCH_2CH$_2$CH$_2$CH$_3$), superimposes 0.90 (t, $J_{vic}=7.3$, 3× SnCH$_2$CH$_2$CH$_2$CH_3), 1.32 (tq, both $J_{vic}=7.4$ 3×SnCH$_2$CH$_2$CH_2CH$_3$), 1.43–1.58 (m, 3×SnCH$_2$CH_2CH$_2$CH$_3$), 5.89 (d, $J_{1',2'}=11.7$, 1′-H)*, 6.14 (d, $J_{3,4}=5.2$, 3-H), AB signal ($\delta_A=6.31$, $\delta_B=6.36$, $J_{AB}=14.7$, in addition split by $J_{A,3'}=9.9$, $J_{B,6'}=9.2$, A: 4′-H, B: 5′-H)*, 6.49 (d, $J_{7',6'}=18.8$, 7′-H)*, superimposes high-field peak of 6.53 (dd, $J_{3',2'}=14.9$, $J_{3',4'}=9.8$, 3′-H)*, 6.65 (dd, $J_{6',7'}=18.6$, $J_{6',5'}=9.4$, 6′-H)*, 6.75 (dd, $J_{2',3'}=14.9$, $J_{2',1'}=11.7$, 2′-H)*, 7.36 (d, $J_{4,3}=5.2$, 4-H); *distinguishable by a H,H correlation spectrum; ^{1}H NMR (500 MHz, C_6D_6; contains 2 mol% *t*BuOMe): $\delta=0.94$ (t, $J_{vic}=7.4$, 3×SnCH$_2$CH$_2$CH$_2$CH_3), 0.97–1.04 (m, 3×SnCH_2CH$_2$CH$_2$CH$_3$), 1.38 (tq, both $J_{vic}=7.4$, 3×SnCH$_2$CH$_2$CH_2CH$_3$), 1.52–1.68 (m, 3× SnCH$_2$CH_2CH$_2$CH$_3$), 5.15 (d, $J_{1',2'}=11.7$, 1′-H)*, 5.50 (d, $J_{3,4}=5.5$, 3-H), 6.05 (ddd, $J_{4',5'}=14.8$, $J_{4',3'}=11.2$, $^4J_{4',6'}=0.5$, 4′-H)*, 6.19 (dd, $J_{3',2'}=14.8$, $J_{3',4'}=11.2$, 3′-H)*, 6.283 (d, $J_{4,3}=5.2$, 4-H), also superimposes 6.283 (!) (ddd, only peaks #1, #2, #5, #7 and #8 of this signal visible, $J_{5',4'}\approx14.8$, $J_{5',6'}\approx10.3$, $J_{allyl}\approx0.7$, 5′-H)*, 6.55 (d, $J_{7',6'}=18.6$, each peak flanked by Sn isotope satellites as 1 unresolved d, $^2J_{^{119}Sn,7'}\approx{}^2J_{^{117}Sn,7'}\approx66.4$, 7′-H)*, 6.68 (dd, $J_{2',3'}=14.8$, $J_{2',1'}=11.6$, 2′-H)*, 6.77 (ddd, $J_{6',7'}=18.5$, $J_{6',5'}=10.0$, $^4J_{6',4'}=0.5$, 6′-H)*; *distinguishable by a H,H correlation spectrum; ^{13}C NMR (125 MHz, C_6D_6): $\delta=9.92$ (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1''}=344.5$, $^1J_{^{117}Sn,C\text{-}1''}=329.1$, Sn$CH_2CH_2CH_2CH_3$), 13.90 (SnCH$_2CH_2CH_2CH_3$), 27.67 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3''}={}^3J_{^{117}Sn,C\text{-}3''}=54.2$, SnCH$_2CH_2CH_2CH_3$), 29.54 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2''}={}^2J_{^{117}Sn,C\text{-}2''}=20.9$, SnCH$_2CH_2CH_2CH_3$), 113.95 (C-1′)*, 118.45 (C-3)*, 126.57 (C-2′)*, 132.17 (C-4′)*, 138.35 (C-3′)*, 138.46 (C-7′)*, 138.81 and 141.93 (C-4, C-5′)*, 147.38 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}6'}={}^2J_{^{117}Sn,C\text{-}6'}=9.1$, C-6′)*, 149.30 (C-5), 168.64 (C-1); *assignment by a C,H correlation spectrum; IR ($CDCl_3$): $\tilde{\nu}=2960$, 2930, 2870, 2860, 1775, 1750, 1595, 1580, 1545, 1530, 1335, 1150, 1110, 1065 cm^{-1}; elemental analysis calcd (%) for $C_{23}H_{36}O_2Sn$ (462.2): C 59.63, H 7.83; found: C 59.86, H 7.70.

***trans*-(1-Phenyl-1,2,3,4-tetrazol-5-yl) [3-(tributylstannyl)-2-propenyl] sulfide (33a)**: At 0°C 1-phenyl-1*H*-tetrazole-5-thiol (385 mg, 2.16 mmol, 1.06 equiv), PPh_3 (590 mg, 2.25 mmol, 1.10 equiv) and DEAD (389 mg, 2.23 mmol, 1.09 equiv) were added to a solution of alcohol **17** (708.8 mg, 2.042 mmol) in THF (8 mL). After 3 h the solvent was evaporated in vacuo and the residue purified by flash chromatography (3 cm, cyclohexane/EtOAc/NEt_3 500:10:10, product in #5–14) to afford the title compound (956 mg, 92%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.81$–0.95 (m, 3×SnCH_2CH$_2$CH$_2$CH$_3$ and 3×SnCH$_2$CH$_2$CH$_2$CH_3), 1.28 (tq, both $J_{vic}=7.2$, 3×SnCH$_2$CH$_2$CH_2CH$_3$), 1.37–1.54 (m, 3× SnCH$_2$CH_2CH$_2$CH$_3$), 4.08 (m; the 4 highest paeks presumably interpretable as dd, $J_{1',2'}=6.5$, $J_{allyl}=1.2$, flanking peaks probably due to $^4J_{Sn,H}$, 1′-H$_2$), 6.07 (dt, $J_{2',3'}=18.6$, $J_{2',1'}=6.5$, each peak flanked by Sn isotope satellites as 2 interlocked d, $^3J_{^{119}Sn,H}=57.8$, $^3J_{^{117}Sn,H}=55.1$, 2′-H), 6.35 (dt, $J_{3',2'}=18.8$, $J_{allyl}=1.2$, each peak flanked by Sn isotope satellites as 2 interlocked d, $^2J_{^{119}Sn,H}=66.5$, $^2J_{^{117}Sn,H}=63.8$, 3′-H), 7.52–7.60 (m, C_6H_5); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=9.52$ (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1''}=346.7$, $^1J_{^{117}Sn,C\text{-}1''}=331.2$, Sn$CH_2CH_2CH_2CH_3$), 13.65 (SnCH$_2CH_2CH_2CH_3$), 27.18 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3''}={}^3J_{^{117}Sn,C\text{-}3''}=54.8$, SnCH$_2CH_2CH_2CH_3$), 28.98 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2''}={}^2J_{^{117}Sn,C\text{-}2''}=20.9$, SnCH$_2CH_2CH_2CH_3$), 38.99 (C-1′)*, 123.88, 129.75 and 130.06 (*each* displays doubled intensity which is surprising in view of assignment as C_{para}, 2×C_{ortho}, 2×C_{meta}, C_{para})*, 133.77 (C_{ipso}), 136.09 (C-3′)*, 139.99 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2'}={}^2J_{^{117}Sn,C\text{-}2'}=9.1$, C-2′)*, 153.94 (C-5); *assignment by a C,H correlation spectrum; IR (film): $\tilde{\nu}=2955$, 2925, 2870, 2850, 1595, 1500, 1465, 1410, 1385, 1280, 1245, 1075, 1050, 1015, 985, 875, 760, 695, 600, 460 cm^{-1}; elemental analysis calcd (%) for $C_{22}H_{36}N_4SSn$ (508.2): C 52.08, H 7.15, N 11.04, S 6.32; found: C 52.20, H 7.19, N 11.09, S 6.39.

***trans*-(Benz-1,3-thiazol-2-yl) [3-(tributylstannyl)-2-propenyl] sulfide (33b)**: At 0°C benz-1,3-thiazole-2-thiol (489 mg, 2.93 mmol, 1.05 equiv), PPh_3 (802 mg, 3.06 mmol, 1.10 equiv), and DEAD (530 mg, 3.05 mmol, 1.09 equiv) were added to a solution of alcohol **17** (966.0 mg, 2.784 mmol) in THF (12 mL). After 1 h the solvent was evaporated in vacuo and the residue purified by flash chromatography (3 cm, cyclohexane/NEt_3 200:4, product in #5–9) to afford the title compound (1.326 g, 96%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=0.80$–0.94 (m, 3× SnCH_2CH$_2$CH$_2$CH$_3$), superimposes 0.85 (t, $J_{vic}=7.3$, 3× SnCH$_2$CH$_2$CH$_2$CH_3), 1.26 (tq, both $J_{vic}=7.3$, 3×SnCH$_2$CH_2CH$_2$CH$_3$), 1.38–1.52 (m, 3×SnCH$_2$CH$_2$CH_2CH$_3$), 4.03 (dd, $J_{1',2'}=6.4$, $J_{allyl}=1.3$, each peak flanked by Sn isotope satellites as 1 d, $^4J_{^{119}Sn,H}={}^4J_{^{117}Sn,H}=2.7$, 1′-H$_2$), 6.10 (dt, $J_{trans}=18.5$, $J_{2',1'}=6.3$, each peak flanked by Sn isotope satellites as 2 interlocked d, $^3J_{^{119}Sn,H}=58.6$, $^3J_{^{117}Sn,H}=56.1$, 2′-H), 6.34 (dt, $J_{trans}=18.9$, $J_{allyl}=1.3$, each peak flanked by Sn isotope satellites as 2 interlocked d, $^2J_{^{119}Sn,H}=68.1$, $^2J_{^{117}Sn,H}=65.4$, 3′-H), 7.29 (ddd, $J_{6,7}=8.1$, $J_{6,5}=7.2$, $^3J_{6,4}=1.2$, 6-H)*, 7.41 (ddd, $J_{5,4}=8.2$, $J_{5,6}=7.2$, $^3J_{5,7}=1.1$, 5-H)*, 7.75 (ddd, $J_{7,6}=8.0$, $^3J_{7,5}=1.2$, $^4J_{7,4}=0.6$, 7-H**, 7.87 (ddd, $J_{4,5}=8.2$, $^3J_{4,6}=1.2$, $^4J_{4,7}=0.6$, 4-H)**; *,**interchangeable; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=9.52$ (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1''}=345.4$, $^1J_{^{117}Sn,C\text{-}1''}=330.1$,

$SnCH_2CH_2CH_2CH_3$), 13.64 ($SnCH_2CH_2CH_2CH_3$), 27.19 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3''} = {}^3J_{^{117}Sn,C\text{-}3''} = 53.9$, $SnCH_2CH_2CH_2CH_3$), 29.00 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2''} = {}^2J_{^{117}Sn,C\text{-}2''} = 20.9$, $SnCH_2CH_2CH_2CH_3$), 39.57 (C-1′)*, 120.87 (C-7)*,**, 121.57 (C-4)*,**, 124.17 and 125.99 (C-5, C-6)*, 134.78 (C-3′)*, 135.33 (C-7a), 140.90 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2'} = {}^2J_{^{117}Sn,C\text{-}2'} = 8.8$, C-2′)*, 153.29 (C-3a), 166.57 (C-2); *interchangeable; **assignment by a C,H correlation spectrum; IR (film): $\tilde{\nu}$ = 2955, 2925, 2850, 1590, 1460, 1430, 1375, 1310, 1240, 1075, 995, 875, 755, 725, 670, 595 cm^{-1}; elemental analysis calcd (%) for $C_{22}H_{35}NS_2Sn$ (497.1):C 53.23, H 7.11, N 2.82, S 12.92; found: C 53.28, H 7.09, N 2.72, S 12.63.

***trans*-(Benz-1,3-thiazol-2-yl)-[3-(tributylstannyl)-2-propenyl]sulfone (34b)**: At 0 °C a solution of $(NH_4)_6Mo_7O_{24}$ (648.7 mg, 0.5253 mmol, 0.20 equiv) in H_2O_2 (30 % in H_2O, 2.68 mL, 26.3 mmol, 10.0 equiv) was added to a solution of sulfide **33b** (1.304 g, 2.623 mmol) in EtOH (12 mL). After 2 h it was diluted with *t*BuOMe (10 mL) and H_2O (10 mL) was added. The organic phase was extracted with *t*BuOMe (2 × 10 mL). The combined organic phases were washed with aq. $NaHSO_3$ (3 × 5 mL). The organic phase was concentrated in vacuo to half of its volume and dried with Na_2SO_4. Evaporation of the solvent in vacuo afforded the title compound (1.152 g, 83 %) as a yellow solid (m.p. 42–44 °C) which was used in the next reaction without further purification; ^{1}H NMR (300 MHz, $CDCl_3$, slightly contaminated in the aliphatic region): δ = 0.67–0.95 (m, 3 × $SnCH_2CH_2CH_2CH_3$), superimposes 0.82 (t, J_{vic} = 7.2, 3 × $SnCH_2CH_2CH_2CH_3$), 1.19 (tq, both J_{vic} = 7.2, 3 × $SnCH_2CH_2CH_2CH_3$), 1.29–1.45 (m, 3 × $SnCH_2CH_2CH_2CH_3$), 4.29 (dd with broad stump due to unresolved $^4J_{Sn,H}$ coupling, $J_{1',2'}$ = 6.7, J_{allyl} = 1.0, 1′-H), 5.96 (dt, J_{trans} = 18.9, $J_{2',1'}$ = 6.8, each peak flanked by Sn isotope satellites as 2 interlocked d, $^3J_{^{119}Sn,H} = 61.3$, $^3J_{^{117}Sn,H} = 59.3$, 2′-H), 6.32 (d with unresolved allyl coupling, J_{trans} = 18.9, each peak flanked by Sn isotope satellites as 2 interlocked d, $^2J_{^{119}Sn,H} = 62.1$, $^2J_{^{117}Sn,H} = 59.8$, 3′-H), 7.61 (m, 5-H, 6-H), 7.99 (m, 7-H)*, 8.23 (m, 4-H)*; *interchangeable; ^{13}C NMR (125 MHz, $CDCl_3$; slightly contaminated): δ = 9.47 (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1''} = 348.5$, $^1J_{^{117}Sn,C\text{-}1''} = 333.0$, $SnCH_2CH_2CH_2CH_3$), 13.56 ($SnCH_2CH_2CH_2CH_3$), 27.09 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3''} = {}^3J_{^{117}Sn,C\text{-}3''} = 55.7$, $SnCH_2CH_2CH_2CH_3$), 28.81 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2''} = {}^2J_{^{117}Sn,C\text{-}2''} = 21.2$, $SnCH_2CH_2CH_2CH_3$), 62.23 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}1'} = {}^3J_{^{117}Sn,C\text{-}1'} = 61.8$, C-1′)*, 122.16 and 125.44 (C-4, C-7)*, 127.54 and 127.91 (C-5, C-6)*, 131.11 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2'} = {}^2J_{^{117}Sn,C\text{-}2'} = 12.7$, C-2′)*, 136.80 (C-7a), 145.13 (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}3'} = 325.8$, $^1J_{^{117}Sn,C\text{-}3'} = 311.2$, C-3′)*, 152.67 (C-3a), 165.28 (C-2)*; *assignment by a C,H correlation spectrum; IR (KBr): $\tilde{\nu}$ = 2960, 2925, 2870, 2860, 1470, 1460, 1420, 1375, 1340, 1320, 1240, 1150, 1125, 1025, 1000, 890, 765, 730, 705, 690 cm^{-1}; (m/z) = 472.04269 ± 5 mDa [M^+] confirmed by HRMS (EI, 70 eV); elemental analysis calcd (%) for $C_{22}H_{35}NO_2S_2Sn$ (529.1): C 50.01, H 6.68, N 2.65, S 12.14; found: C 49.69, H 6.66, N 4.15, S 11.48.

1-*trans*,3-*cis*,5-*trans*-1,6-Bis(tributylstannyl)-1,3,5-hexatriene (*trans*,*cis*,*trans*-35): At −78 °C KHDMS (1.0 M in THF, 0.47 mL, 0.47 mmol, 1.20 equiv) was added to a solution of aldehyde **18** (136 mg, 0.391 mmol) and sulfone **34b** (265 mg, 0.502 mmol, 1.28 equiv) in THF (5 mL), giving an orange solution. After warming to room temperature overnight, the solution was diluted with *t*BuOMe (8 mL) and H_2O (8 mL) was added. The aq. phase was extracted with *t*BuOMe (3 × 6 mL). The combined organic phases were washed with brine (4 mL). After drying with Na_2SO_4 the solvent was evaporated in vacuo to afford an oily residue, which was purified by flash chromatography [2.5 cm, Al_2O_3 (desactivated with 2 % H_2O), cyclohexane/NEt_3 200:4, product in #3–5]. The title compound (169 mg, 66 %) and its 3-*trans*-isomer (4 mg, 3 %) were obtained as an inseparable slightly yellow oil. The *cis*/*trans* ratio was determined from ^{1}H NMR integrals of *cis*-3-H/*cis*-4-H (δ = 5.90), *cis*-1-H/*cis*-6-H (δ = 6.32), *cis*-2-H/*cis*-5-H (δ = 7.08) and *trans*-3-H/*trans*-4-H (δ = 6.15), *trans*-2-H/*trans*-5-H (δ = 6.55); ^{1}H NMR (500 MHz, CDCl): δ = 0.86–0.99 (m, 6 × $SnCH_2CH_2CH_2CH_3$), superimposes 0.90 (t, J_{vic} = 7.2, 6 × $SnCH_2CH_2CH_2CH_3$), 1.32 (tq, both J_{vic} = 7.3, 6 × $SnCH_2CH_2CH_2CH_3$), 1.43–1.59 (m, 6 × $SnCH_2CH_2CH_2CH_3$), 5.90 (m, higher order, 3-H, 4-H), 6.32 (d, $J_{1,2} = J_{6,5}$ = 18.5, each peak flanked by Sn isotope satellites as 2 interlocked d, $^2J_{^{119}Sn,H} = 71.9$, $^2J_{^{117}Sn,H} = 68.9$, 1-H*, 6-H*), 7.08 (m, higher order, each peak flanked by Sn isotope satellites, which are not exactly interpretable, 2-H*, 5-H*); *distinguishable by a H,H correlation spectrum; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 9.59 (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1'} = {}^1J_{^{119}Sn,C\text{-}1''} = 344.8$, $^1J_{^{117}Sn,C\text{-}1'} = {}^1J_{^{117}Sn,C\text{-}1''} = 329.4$, $SnCH_2CH_2CH_2CH_3$), 13.69 ($SnCH_2CH_2CH_2CH_3$), 27.28 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3'} = {}^3J_{^{119}Sn,C\text{-}3''} = {}^3J_{^{117}Sn,C\text{-}3'} = {}^3J_{^{117}Sn,C\text{-}3''} = 54.2$, $SnCH_2CH_2CH_2CH_3$), 29.12 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2'} = {}^2J_{^{119}Sn,C\text{-}2''} = {}^2J_{^{117}Sn,C\text{-}2'} = {}^2J_{^{117}Sn,C\text{-}2''} = 20.6$, $SnCH_2CH_2CH_2CH_3$), 130.96 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3} = {}^3J_{^{119}Sn,C\text{-}4} = {}^3J_{^{117}Sn,C\text{-}3} = {}^3J_{^{117}Sn,C\text{-}4} = 73.9$, C-3, C-4)*, 136.42 (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1} = {}^1J_{^{119}Sn,C\text{-}6} = 377.2$, $^1J_{^{117}Sn,C\text{-}1} = {}^1J_{^{117}Sn,C\text{-}6} = 360.6$, C-1, C-6)*, 141.89 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2} = {}^2J_{^{119}Sn,C\text{-}5} = {}^2J_{^{117}Sn,C\text{-}2} = {}^2J_{^{117}Sn,C\text{-}5} = 9.7$, C-2, C-5)*; *assignment by a C,H correlation spectrum; the *cis* configuration of the C^3=C^4 double bond was proved by: 1) A SELINCOR experiment (500 MHz/125.7 MHz; $CDCl_3$) revealed the H,H coupling constants $J_{3,4} \approx J_{3,2} = J_{4,5} \approx 10.9$ for the ^{13}C signal at δ = 130.96 (C-3/C-4). 2) An ^{1}H-coupled C,H correlation spectrum (500/125 MHz; $CDCl_3$) revealed the same H,H coupling constants $J_{3,4} \approx J_{3,2} \approx J_{4,5} \approx 10.9$ for the ^{13}C signal at δ = 130.96 (C-3/C-4); IR (film): $\tilde{\nu}$ = 2955, 2925, 2850, 1575, 1465,1385, 1375, 1070, 985, 875, 865, 835, 690, 665, 595, 505 cm^{-1}; elemental analysis calcd (%) for $C_{30}H_{60}Sn_2$ (660.3): C 54.74, H 9.19; found: C 55.01, H 9.35.

all-*trans*-1,6-Bis(tributylstannyl)-1,3,5-hexatriene (*trans*,*trans*,*trans*-35): To a vigorously stirred solution of sulfone **38** (200.0 mg, 0.276 mmol) in THF (3 mL) freshly distilled CBr_2F_2 (0.10 mL, 0.23 g, 1.10 mmol, 4 equiv) was added at 0 °C and in portions KOH [30 % on Al_2O_3; 1.049 g, 5.525 mmol, 20.0 equiv; prepared by adding KOH (315 mg, 5.53 mmol, 20.0 equiv) to a suspension of Al_2O_3 (612 mg, desactivated with 3 % H_2O) in dry MeOH (3 mL); the solvent was evaporated in vacuo and the residue grinded under Ar with a spatula]. After stirring at room temperature for 30 min, the suspension was filtered through a pad of Celite and washed with pentane (12 mL). Evaporation of the solvent afforded an oily residue which was purified by flash chromatography [2.5 cm, Al_2O_3 (desactivated with 3 % H_2O), cyclohexane/EtOAc 500:5, product in #4] to afford the title compound (132.3 mg, 73 %) as a 96:4 mixture [determined from ^{1}H NMR integrals of *trans*-2-H/*trans*-5-H (δ = 6.56), *trans*-3-H/*trans*-4-H (δ = 6.15) and *cis*-2-H/*cis*-5-H (δ = 7.08), *cis* 3-H/*cis*-4-H (δ = 5.90)] as a slightly yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.83–0.97 (m, 6 × $SnCH_2CH_2CH_2CH_3$), superimposes 0.89 (t, J_{vic} = 7.3, 6 × $SnCH_2CH_2CH_2CH_3$), 1.31 (tq, both J_{vic} = 7.3, 6 × $SnCH_2CH_2CH_2CH_3$), 1.41–1.58 (m, 6 × $SnCH_2CH_2CH_2CH_3$), 6.15 (m, higher order, 3-H*, 4-H*), 6.29 (d, $J_{1,2} = J_{6,5}$ = 18.6, each peak flanked by Sn isotope satellites as 2 interlocked d, $^2J_{^{119}Sn,H} = 70.1$, $^2J_{^{117}Sn,H} = 67.2$, 1-H, 6-H), 6.56 (m, higher order, each peak flanked by Sn isotope satellites, which are not exactly interpretable, 2-H*, 5-H*); *distinguished by a H,H correlation spectrum; ^{13}C NMR (125 MHz, $CDCl_3$; slightly contaminated): δ = 9.57 (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1'} = {}^1J_{^{119}Sn,C\text{-}1''} = 344.8$, $^1J_{^{117}Sn,C\text{-}1'} = {}^1J_{^{117}Sn,C\text{-}1''} = 329.4$, 6 × $SnCH_2CH_2CH_2CH_3$), 13.69 (6 × $SnCH_2CH_2CH_2CH_3$), 27.27 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3'} = {}^3J_{^{119}Sn,C\text{-}3''} = {}^3J_{^{117}Sn,C\text{-}3'} = {}^3J_{^{117}Sn,C\text{-}3''} = 54.5$, 6 × $SnCH_2CH_2CH_2CH_3$), 29.10 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2'} = {}^2J_{^{119}Sn,C\text{-}2''} = {}^2J_{^{117}Sn,C\text{-}2'} = {}^2J_{^{117}Sn,C\text{-}2''} = 20.6$, 6 × $SnCH_2CH_2CH_2CH_3$), 134.47 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3} = {}^3J_{^{119}Sn,C\text{-}4} = {}^3J_{^{117}Sn,C\text{-}3} = {}^3J_{^{117}Sn,C\text{-}4} = 73.6$, C-3, C-4)*, 135.57 (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1} = {}^1J_{^{119}Sn,C\text{-}6} = 380.0$, $^1J_{^{117}Sn,C\text{-}1} = {}^1J_{^{117}Sn,C\text{-}6} = 363.3$, C-1, C-6)*, 146.90 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2} = {}^2J_{^{119}Sn,C\text{-}5} = {}^2J_{^{117}Sn,C\text{-}2} = {}^2J_{^{117}Sn,C\text{-}5} = 6.4$, C-2, C-5)*; *assignment by a C,H correlation spectrum; the *trans* configuration of the C^3=C^4 double bond was proved by: 1) A SELINCOR experiment (500 MHz/125 MHz $CDCl_3$) revealed for the ^{13}C signal at δ = 134.47 (C-3/C-4) the H,H coupling constants $J_{3,4}$ = 15.1 and $J_{3,2} = J_{4,5}$ = 10.1. 2) An ^{1}H-coupled C,H correlation spectrum (500/125 MHz, $CDCl_3$) revealed for the ^{13}C signal at δ = 134.47 (C-3/C-4) nearly the same H,H coupling constants $J_{3,4}$ = 15.1 and $J_{3,2} = J_{4,5}$ = 10.3; IR (film): $\tilde{\nu}$ = 2955, 2925, 2870, 2860, 1575, 1465, 1420, 1375, 1340, 1290, 1265, 1180, 1150, 1070, 1045, 1005, 960, 875, 865, 785, 690, 665, 595 cm^{-1}; (m/z) = 603.20347 ±5 mDa [M^+ −Bu] was confirmed by HRMS (Cl, 120 eV); elemental analysis calcd (%) for $C_{30}H_{60}Sn_2$ (660.3): C 54.74, H 9.19; found: C 53.81, H 8.97.

***trans*-3-Bromo-1-(tributylstannyl)propene (36)**:[44] At 0 °C a solution of PPh_3 (1.935 g, 7.385 mmol, 1.10 equiv) in CH_2Cl_2 (8 mL) was added

within 75 min to a solution of alcohol **17** (2.320 g, 6.686 mmol) and CBr_4 (2.672 g, 8.707 mmol, 1.21 equiv) in CH_2Cl_2 (14 mL). After 1 h the solution was concentrated in vacuo to half of its volume and pentane (25 mL) was added. The precipitate was filtered off and the filtrate washed with aq. $NaHCO_3$ (10 mL). After drying with Na_2SO_4 the solvent was evaporated in vacuo to afford an oily residue. Purification by flash chromatography (4.5 cm, cyclohexane, product in #6–10) afforded the title compound (2.247 g, 82%; ref.:[44] 81%) as a colorless oil.

Bis[*trans*-3-(tributylstannyl)-2-propenyl] sulfide (37): A solution of bromide **36** (443.0 mg, 1.056 mmol) in THF (2 mL) was added to a solution of $Na_2S{\cdot}9H_2O$ (126.7 mg, 0.53 mmol, 0.50 equiv) and Bu_4NHSO_4 (2.4 mg, 0.001 mmol, 0.007 equiv) in H_2O (2 mL). After vigorous stirring at room temperature for 18 h, the emulsion was diluted with pentane (6 mL). The aq. phase was extracted with pentane (2×4 mL). The combined organic phases were dried with Na_2SO_4. Evaporation of the solvent in vacuo afforded an oily residue, which was purified by flash chromatography (2.5 cm, cyclohexane/EtOAc 25:1, product in #2–3) to afford the title compound (331.8 mg, 90%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78–1.01 (m, 6×SnCH_2CH$_2$CH$_2$CH$_3$), superimposes 0.89 (t, J_{vic} = 7.2, 6×SnCH$_2$CH$_2$CH$_2$CH_3), 1.31 (tq, both J_{vic} = 7.3, 6×SnCH$_2$CH$_2$CH_2CH$_3$), 1.40–1.62 (m, 6×SnCH$_2$CH_2CH$_2$CH$_3$), 3.14 (d with small extra peak in the middle showing transition to higher order, $J_{1,2}$ = 5.9, 2×1-H$_2$), AB signal (δ_A = 5.85, δ_B = 5.95, J_{AB} = 18.8, in addition split by $J_{A,1}$ = 6.0; each peak of A-part flanked by Sn isotope satellites as 1 dm, but superimposed by the 3-H signal and therefore not exactly interpretable; in B-part each peak flanked by Sn isotope satellites as 1 dm, $^2J_{^{119}Sn,3\text{-}H} \approx {}^2J_{^{117}Sn,3\text{-}H} \approx 72$; A: 2×2-H, B: 2×3-H); IR (film): $\tilde{\nu}$ = 2955, 2925, 2870, 2850, 1590, 1465, 1415, 1375, 1340, 1290, 1240, 1070, 1025, 1000, 985, 960, 875, 865, 690, 665, 615, 595, 505 cm^{-1}; elemental analysis calcd (%) for $C_{30}H_{62}SSn_2$ (694.3): C 52.05, H 9.03, S 4.63; found: C 52.30, H 8.89, S 4.47.

Bis[*trans*-3-(tributylstannyl)-2-propenyl]sulfone (38): At 0 °C a solution of $(NH_4)_6Mo_7O_{24}$ (103.2 mg, 0.0836 mmol, 0.20 equiv) in H_2O_2 (30% in H_2O, 0.39 mL, 3.82 mmol, 9.0 equiv) was added dropwise to a solution of sulfide **37** (294.8 mg, 0.4254 mmol) in EtOH (2 mL). After 15 min the solution was allowed to warm to room temperature and stirred for 1 h at this temperature. It was diluted with *t*BuOMe (2 mL) and pentane (6 mL) and the aq. phase extracted with pentane (3×4 mL). The combined organic phases were washed with aq. $Na_2S_2O_3$ (2 mL) and dried with $MgSO_4$. The solvent was evaporated in vacuo affording an oily residue which was purified by flash chromatography (2.5 cm, cyclohexane/EtOAc 250:10, product in #2–6) to afford the title compound (271.9 mg, 88%) as a colorless oil. ^{1}H NMR (499.9 MHz, $CDCl_3$/TMS): δ = ca. 0.89–1.03 (m, 6×SnCH_2CH$_2$CH$_2$CH$_3$), superimposes 0.90 (t, J_{vic} = 7.4, 6×SnCH$_2$CH$_2$CH$_2$CH_3), 1.31 (tq, both J_{vic} = 7.3, 6×SnCH$_2$CH$_2$CH_2CH$_3$), 1.42–1.58 (m, 6×SnCH$_2$CH_2CH$_2$CH$_3$), 3.74 (d, $J_{1,2}$ = 6.9, 2×1-H$_2$), 6.02 (dt, $J_{2,3}$ = 18.9, $J_{2,1}$ = 6.8, each peak flanked by partly unresolved Sn isotope satellites as 2 interlocked d, $^3J_{^{119}Sn,H}$ = 56.0, $^3J_{^{117}Sn,H} \approx$ 53.5, 2×2-H), 6.41 (d, $J_{3,2}$ = 18.9, each peak flanked von Sn isotope satellites als 2 interlocked d, $^2J_{^{119}Sn,H}$ = 63.6, $^2J_{^{117}Sn,H}$ = 61.2, 2×3-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 9.63 (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}1'}$ = 348.5, $^1J_{^{117}Sn,C\text{-}1'}$ = 332.7, 6×SnCH$_2$CH$_2$CH$_2$CH$_3$), 13.66 (6×SnCH$_2$CH$_2$CH$_2$CH$_3$), 27.22 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}3'} = {}^3J_{^{117}Sn,C\text{-}3'}$ = 55.1, 6×SnCH$_2$CH$_2$CH_2CH$_3$), 29.07 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}3'} = {}^2J_{^{117}Sn,C\text{-}3'}$ = 21.2, 6×SnCH$_2$CH$_2$CH$_2$CH$_3$), 58.86 (flanked by Sn isotope satellites as 1 d, $^3J_{^{119}Sn,C\text{-}1} = {}^3J_{^{117}Sn,C\text{-}1}$ = 60.9, 2×C-1)*, 133.65 (flanked by Sn isotope satellites as 1 d, $^2J_{^{119}Sn,C\text{-}2} = {}^2J_{^{117}Sn,C\text{-}2}$ = 11.8, 2×C-2)*, 142.67 (flanked by Sn isotope satellites as 2 d, $^1J_{^{119}Sn,C\text{-}3}$ = 330.0, $^1J_{^{117}Sn,C\text{-}3}$ = 315.5, 2×C-3)*; *assignment by a C,H correlation spectrum; IR (film): $\tilde{\nu}$ = 2955, 2925, 2870, 2850, 1595, 1460, 1375, 1330, 1305, 1140, 1115, 1075, 990, 880, 690, 670, 610, 510 cm^{-1}; elemental analysis calcd (%) for $C_{30}H_{62}O_2SSn_2$ (726.3): C 49.75, H 8.63, S 4.43; found: C 49.57, H 8.54, S 4.22.

***trans*-7-Bromo-2-heptene-4,6-diyn-1-ol (39)**: A mixture of NBS (266.8 mg, 1.499 mmol, 1.30 equiv) and $AgNO_3$ (15.7 mg, 92.3 μmol, 0.08 equiv) was added to a solution of alcohol **25** (122.4 mg, 1.153 mmol, together with 0.130 g EtOAc) in degassed acetone (8 mL). After stirring for 13 h under exclusion of light the reaction was terminated by addition of H_2O (5 mL). The aq. phase was extracted with EtOAc (5×10 mL). The combined organic phases were dried with $MgSO_4$. Evaporation of the solvent in vacuo afforded a residue which was purified by flash chromatography (2 cm, desactivated with 3% NEt_3, cyclohexane/EtOAc 5:1, #13–23 cyclohexane/EtOAc 2:1, product in #17–23). The title compound (167.5 mg, 79%) was obtained as a brown solid. M.p. 68 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.51 (br s, OH), 4.25 (dd, $J_{1,2}$ = 4.84, J_{allyl} = 2.1, 1-H$_2$), 5.79 (dt, $J_{3,2}$ = 16.0, J_{allyl} = 2.1, 3-H), 6.45 (dt, $J_{2,3}$ = 16.0, $J_{2,1}$ = 4.8, 2-H); ^{13}C NMR (75.4 MHz, $CDCl_3$/$CDCl_3$): δ = 44.12, 65.36, 72.31 and 74.86 (C-4, C-5, C-6, C-7), 62.66 (C-1), 108.26 (C-3)*, 146.52 (C-2)*; *assignment is based on increment calculation[60] which predicts δ = 108.9 (C-3) and δ = 143.4 (C-2); IR ($CDCl_3$): $\tilde{\nu}$ = 3620, 3155, 2920, 2860, 2255, 2130, 1795, 1685, 1655, 1560, 1540, 1510, 1475, 1460, 1450, 1420, 1380, 1295, 1215, 1190 1090, 1015, 945, 935 cm^{-1}; elemental analysis calcd (%) for C_7H_5BrO (184.0): C 45.44, H 2.72; found: C 45.22, H 2.82.

***trans*-7-Bromo-2-heptene-4,6-diynal (40)**: At 0 °C Dess–Martin periodinane (429.5 mg, 1.1013 mmol, 1.52 equiv) was added to a solution of alcohol **39** (133.1 mg, 0.7234 mmol) in CH_2Cl_2 (6 mL). The solution was allowed to warm to room temperature within 2.5 h. Evaporation of the solvent in vacuo afforded a residue which was purified by flash chromatography (2.5 cm, cyclohexane/EtOAc 5:1, product in #2–9) to afford the title compound (104.0 mg, 79%) as a brown solid [m.p. 111 °C (decomp.)] which rapidly turned dark; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.59 (d*, J = 3.8, 2-H, 3-H), 9.59 (dd*, $^2J_{1,2} = {}^3J_{1,3}$ = 3.7, 1-H); *presumably "deceptively simple spectrum" instead of first-order spectrum; $J_{2,3}$ determined by ^{1}H NMR (300 MHz, C_6D_6): δ = 5.42 (d, $J_{3,2}$ = 16.0, 3-H), 6.01 (dd, $J_{2,3}$ = 16.0, $J_{2,1}$ = 7.5, 2-H), 8.83 (d, $J_{1,2}$ = 7.5, 1-H); ^{13}C NMR (75.4 MHz, $CDCl_3$/$CDCl_3$): δ = 51.96, 64.71, 69.69 and 87.81 (C-4, C-5, C-6, C-7), 130.02 (C-3)*, 142.36 (C-2)*, 192.40 (C-1); *assignment is based on increment calculation[60] which predicts δ = 131.8 (C-3) and δ = 144.5 (C-2); IR ($CDCl_3$): $\tilde{\nu}$ = 3155, 2980, 2825, 2735, 2255, 2210, 1795, 1685, 1650, 1595, 1560, 1470, 1385, 1290, 1255, 1215, 1165, 1120, 955, 925, 885, 770, 750, 725 cm^{-1}; elemental analysis calcd (%) for C_7H_3BrO (181.9): C 45.94, H 1.65; found: C 45.71, H 1.66.

1,3-Heptadiyne (41):[3]

1-Iodo-1,3-heptadiyne (42):[3]

***trans*-7-Bromo-2-heptene-4,6-diynoic acid (43)**: To a solution of aldehyde **42** (105.3 mg, 0.5757 mmol) in degassed acetone (12 mL) 2-methyl-2-butene (0.23 mL, 2.0 mmol, 3.5 equiv) and a solution of $NaClO_2$ (80%, 137.7 mg, 1.209 mmol, 2.10 equiv) and KH_2PO_4 (195.7 mg, 1.439 mmol, 2.50 equiv) in H_2O (8 mL) were added at 0 °C. After 1 h H_2O (10 mL) was added and the solution acidified to pH 2 with HCl (1 M). After extraction with EtOAc (5×5 mL) the combined organic phases were washed with brine (2×5 mL) and dried with $MgSO_4$. Evaporation of the solvent in vacuo afforded a residue which was purified by flash chromatography (2.5 cm, EtOAc, product in #2–7) to afford the title compound (100.9 mg, 89%) as a brown solid. M.p. 128 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.37 (d, $J_{2,3}$ = 15.8, 2-H), 6.83 (d, $J_{3,2}$ = 15.8, 3-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 49.99, 64.82, 70.07 and 84.07 (C-4, C-5, C-6, C-7), 125.89 (C-3), 132.86 (C-2), 169.68 (C-1); IR ($CDCl_3$): $\tilde{\nu}$ = 3155, 2985, 2900, 1815, 1795, 1695, 1615, 1470, 1380, 1300, 1215, 1095, 885 cm^{-1}; (m/z) = 197.93164 ± 5 mDa [M^+], confirmed by HRMS (EI, 70 eV); elemental analysis calcd (%) for $C_7H_3BrO_2$ (197.9): C 42.25, H 1.52; found: C 42.72, H 1.84.

***trans*-7-Bromo-2-heptene-4,6-diynoic acid 2-(trimethylsilyl)ethyl ester (44)**: To a degassed solution of acid **43** (60.0 mg, 0.302 mmol) in EtOAc (2 mL) 2-(trimethylsilyl)ethanol (50 μL, 41 mg, 0.35 mmol, 1.2 equiv), DCC (4.87 M in THF, 65 μL, 0.32 mmol, 1.1 equiv), and DMAP (1.8 mg, 0.015 mmol, 0.05 equiv) were added at 0 °C. After 1 h the solution was allowed to warm to room temperature and stirred for 1 h at this temperature. H_2O (4 mL) was added and the aq. phase extracted with *t*BuOMe (3×2 mL). The combined organic phases were washed with H_2O (2 mL) and dried with Na_2SO_4. Evaporation of the solvent in vacuo afforded a residue which was purified by flash chromatography (2.5 cm, cyclohexane/EtOAc 30:1, product in #2) to afford the title compound (74.7 mg, 83%) as a brown, instable oil, which was immediately used in the next reaction. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, $SiMe_3$), 1.02 (m, 2′-H$_2$), 4.26 (m, 1′-H$_2$), 6.35 (d, $J_{2,3}$ = 15.8, 2-H), 6.72 (d, $J_{3,2}$ = 16.0, 3-H); IR

(film): $\tilde{\nu}$ = 3265, 2955, 2885, 2120, 1740, 1725, 1710, 1375, 1310, 1235, 1180, 1065, 1045, 965, 935, 910, 870, 755 cm^{-1}; m/z = 315.9 [$M(^{79}Br)^+ + NH_4$], 317.8 [$M(^{81}Br)^+ + NH_4$] confirmed by MS (DCI, NH_3); due to the instability of this compound, it was directly used in the next reaction without further analysis.

Xerulinic acid 2-(trimethylsilyl)ethyl ester (45) [numbering analogous to xerulinic acid (**3**)]: A mixture of [$Pd(dba)_2$] (12.1 mg, 21.0 μmol, 0.06 equiv) and $AsPh_3$ (20.6 mg, 67.3 μmol, 0.19 equiv) was added to a degassed solution of stannane *trans,trans,trans*-**32** (161.1 mg, 0.3470 mmol) and bromide **44** (112.2 mg, 0.3744 mmol, 1.08 equiv) in THF (4 mL). After stirring for 5 h under exclusion of light the solvent was evaporated in vacuo to afford a residue which was purified by repeated flash chromatography (2.5 cm, desactivated with cyclohexane/EtOAc/NEt_3 200:20:8, chromatography with cyclohexane/EtOAc 200:20, #10–22 cyclohexane/EtOAc 200:40, #23–36 cyclohexane/EtOAc 200:60, #37–44 cyclohexane/EtOAc 200:100, product in #35–44) to afford the title compound (99.1 mg, 73%) as a red solid. M.p. 139–140 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.05 (s, $SiMe_3$), 1.03 (m, CH_2SiMe_3), 4.26 (m, OCH_2), 5.78 (d, $J_{11,10}$ = 15.4, 11-H), 5.89 (d, $J_{5,6}$ = 11.7, 5-H), 6.20 (d, $J_{2,3}$ = 5.4, 2-H), 6.32 (d, $J_{17,16}$ = 16.0, 17-H), 6.41–6.56 (m, 7-H, 8-H, 9-H), 6.80–6.88 (m, 6-H, 10-H, 16-H), 7.37 (d, $J_{3,2}$ = 5.2, 3-H); a short-range H,H correlation spectrum (500 MHz, $CDCl_3$) shows, amongst others, cross-peaks between the following resonances: 11-H (δ = 5.78) ⇔ 10-H (δ = 6.80–6.88); 5-H (δ = 5.89) ⇔ 6-H (δ = 6.80–6.88); 2-H (δ = 6.20) ⇔ 3-H (δ = 7.37); 17-H (δ = 6.32) ⇔ 16-H (δ = 6.80–6.88); 6-H, 10-H, 16-H (δ = 6.80–6.88) ⇔ 7-H, 8-H (δ = 6.41–6.56); ^{13}C NMR (125 MHz, $CDCl_3$): δ = −1.50 [$Si(CH_3)_3$], 17.29 (C-2″), 63.31 (C-1″), 78.27, 80.43, 82.45 and 85.31 (C-12, C-13, C-14, C-15), 111.10 (C-11), 114.44 (C-5), 119.14 (C-2), 123.56 (C-16)*, 128.40 (C-6)*, 133.01 (C-17), 134.61 (C-9)**, 136.62 (C-8)**, 137.47 (C-7)**, 142.53 (C-3), 145.27 (C-10)*, 149.73 (C-4)***, 165.52 (C-18)***, 169.18 (C-1)***; *distinguished by a ^{1}H-coupled short-range C,H correlation spectrum; **·***assignment by a long-range C;H correlation spectrum; a short-range C,H correlation spectrum (500 MHz/125 MHz, $CDCl_3$) shows cross-peaks between the following resonances: 11-H (δ = 5.78) ⇔ C-11 (δ = 111.10), 5-H (δ = 5.89) ⇔ C-5 (δ = 114.44), 2-H (δ = 6.20) ⇔ C-2 (δ = 119.14), 17-H (δ = 6.32) ⇔ C-17 (δ = 133.01), 7-H, 8-H, 9-H (δ = 6.41–6.56) ⇔ C-9 (δ = 134.47), C-8 (δ = 136.62), C-7 (δ = 137.47), 6-H, 10-H (δ = 6.80–6.88) ⇔ C-6 (δ = 128.40) and C-10 (δ = 145.27), 16-H (δ = 6.82) ⇔ C-16 (δ = 123.56), 3-H (δ = 7.37) ⇔ C-3 (δ = 142.53). A ^{1}H-coupled short-range C,H correlation (500 MHz/125 MHz) revealed, amongst others: δ = 6.44 (ddd, $^1J_{H,C}$ = 156.3 Hz, $J_{9,8}$ = 12.8 Hz, $J_{9,10}$ = 12.0 Hz, 9-H), δ = 6.51 (ddd, $^1J_{H,C}$ = 156.6 Hz, $J_{8,9}$ = 14.6 Hz, $J_{8,7}$ = 11.6 Hz, 8-H), δ = 6.53 (ddd, $^1J_{H,C}$ = 154.3 Hz, $J_{7,6}$ = 15.2 Hz, $J_{7,8}$ = 11.3 Hz, 7-H), 6.82 (dd, $^1J_{H,C}$ = 168.7 Hz, $J_{16,17}$ = 16.1 Hz, 16-H), δ = 6.85 (ddd, $^1J_{H,C}$ = 157.6 Hz, $J_{10,11}$ = 15.1 Hz, $J_{10,9}$ = 11.1 Hz 10-H), δ = 6.86 (ddd, $^1J_{H,C}$ = 159.2 Hz, $J_{6,7}$ = 13.7 Hz, $J_{6,5}$ = 12.3 Hz, 6-H). A long-range C,H correlation spectrum (500 MHz/125 MHz, $CDCl_3$) shows (amongst others) cross-peaks between the following resonances: δ = 6.20 (2-H) ⇔ δ = 142.53 (C-3), 149.73 (C-4), 169.18 (C-1); δ = 7.37 (3-H) ⇔ δ = 149.73 (C-4), 169.18 (C-1); δ = 5.89 (5-H) ⇔ δ = 137.47 (C-7), 142.53 (C-3), 149.73 (C-4); δ = 111.10 (11-H) ⇔ δ = 145.27 (C-10), δ = 134.61 (C-9); IR (C_6D_6): $\tilde{\nu}$ = 3235, 2290, 2275, 2260, 1780, 1715, 1620, 1615, 1455, 1335, 1320, 1260, 1250, 1165, 1000, 935, 880, 820, 810 cm^{-1}; UV (MeOH): λ_{max} (lg ε) = 416 (4.83), 438 nm (4.78); (m/z) = 392.14439 ± 5 mDa [M^+] confirmed by HRMS (EI, 70 eV); elemental analysis calcd (%) for $C_{23}H_{24}O_4Si$ (392.1): C 70.38, H 6.16; found: C 70.15, H 6.13.

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