50. Palladium-Catalyzed Ene-Type Cyclizations of Terpenoid 1,6-Enynes

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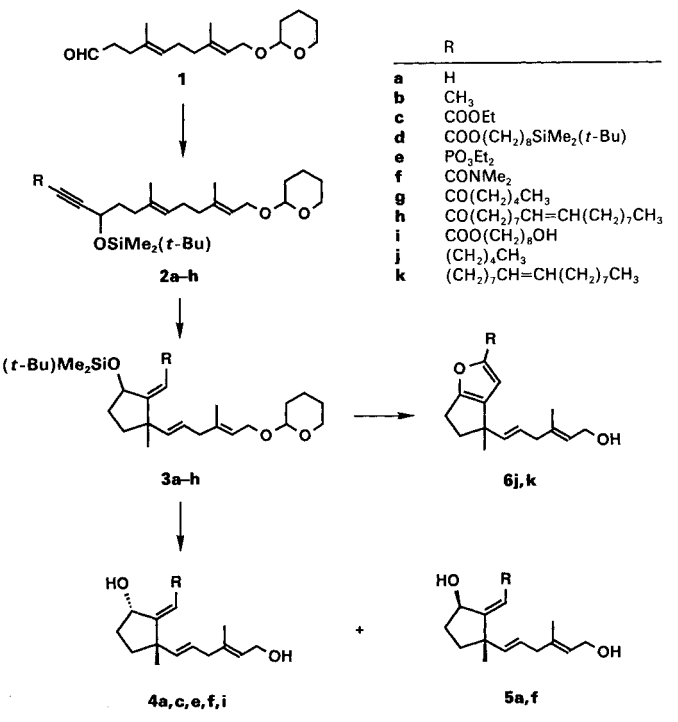
Palladium-catalyzed ene-type cyclizations of 1,6-enynes **2** yield methylidene-cyclopentane derivatives **3**. Removal of protecting groups from **3** furnishes the diols **4** and **5**, whose configurations were established by a combination of X-ray and ^{1}H-NMR techniques. The predominant formation of isomers **4** is discussed in the context of two alternative hypothetical mechanisms previously proposed for this type of cyclization.

1. Introduction. – The discovery of significant ulcer healing properties in modified acyclic terpenes has led to substantial efforts in their synthesis as well as in their pharmacological characterization [1] [2]. Our interest in this area has focussed on substituted farnesyl derivatives bearing a polar group at each end of a C_{10} chain [3]. To gain insight into their possible mechanisms of action, we investigated the chemical reactivity of some of the more active compounds of this series. This has already resulted in the discovery of an acetylenic acetal isomerization [4], a synthesis of halogenated furans [5], and an ynol-to-enone rearrangement [6].

Within this context, we decided to evaluate the propensity of a selected set (**2a–h**) of these terpenoids towards intramolecular cyclizations. This series shares an 1,6-enyne unit embedded into other functionalities. 1,6-Enynes are known to undergo *Alder*-ene reactions involving the acetylene function as the enophile to yield cyclopentanes containing an exocyclic C=C bond (for reviews, *cf.* [7] [8]). Resembling truncated prostaglandin derivatives, these molecules might advantageously combine the cytoprotective properties of the open-chain terpenoids with the antisecretory (gastric acid secretion inhibitory) activity [9] claimed for a large number of synthetic prostanoids [10]. Unfortunately, the desired pharmacological effect was not observed. We do, however, wish to document the cyclopentane synthesis, since it represents a useful extension of a known reaction to hitherto unemployed polyfunctional substrates. Given their relative ease of preparation, this type of cyclopentane may also serve as attractive intermediate in the synthesis of more elaborate prostanoids.

2. Results. – The Pd-catalyzed intramolecular ene-type cyclization of enynes **2** yields methylidene-cyclopentane derivatives **3** (*Scheme*). The starting enynes **2a–d** were prepared by low-temperature addition of the corresponding (substituted) acetylides to the known [11] aldehyde **1**, followed by standard *O*-silylation of the intermediate propargylic alcohol. Compound **2a** was further elaborated into **2e–h** by lithiation and subsequent quenching with the appropriate acid derivative. In a similar manner, aldehyde **1** was converted into **7a, b** by MnO_2 oxidation following acetylide or methyl-acetylide addition and into α,β-unsaturated ester **8** by a 3-nitropropionate addition/β-elimination/silylation sequence. Compounds **2** and **8** represent mixtures of racemic diastereoisomers that are not discriminated by ^{1}H-NMR spectroscopy.

Scheme



Intramolecular ene reactions of 1,6-enynes are known and have, in the past, been accomplished either thermally [7] or under transition-metal catalysis. In a series of papers, *Trost* [8] has scrutinized the chemistry of enynes in the presence of Pd compounds and recommended various catalyst systems for different modes of intramolecular cyclizations. In our studies, we employed catalytic amounts (5%) of $Pd(OAc)_2$ in the presence of Ph_3P (6%). Toluene was used as the solvent and slight heating (50–70°) was usually applied, since the cyclizations are somewhat too slow at room temperature (*e.g.* 30% conversion for **2c** → **3c** after 48 h) to reach completion within practical times. In general, no systematic variation of the catalyst system was carried out. Selected examples do, however, indicate the superiority of $Pd(OAc)_2$ over $Pd(dba)_2$, $PdCl_2(CH_3CN)_2$, and

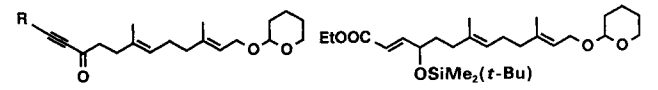
Table 1. *Ene Reaction of Enynes* **2** *in the Presence of* $Pd(OAc)_2$ (5%) *and* Ph_3P (6%)

Substrate	Conditions		Product	Yield [%]
	Temp. [°]	Time [h]		
2a	25	15	**3a**	60
2c	70	19	**3c**	66
2d	75	7	**3d**	69
2e	60	4	**3e**	68
2f	50	24	**3f**	55
2g	50	15	**3g**	81
2h	60	12	**3h**	36

$Pd(Ph_3P)_4$ for this particular purpose. Ph_3P gave the best results among the ligands employed, surpassing Bu_3P, 1,2-bis(diphenylphosphino)ethane, and tris[4-(dimethylamino)phenyl]phosphine, that were ineffective at room temperature.

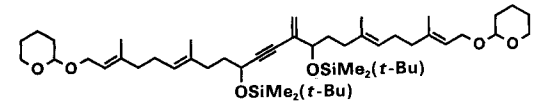
The yields given in *Table 1* refer to isolated products from g-scale reactions. Actual conversion yields are surmised to be consistently higher. However, they could not be quantified by GC due to the thermal lability of the THP (tetrahydropyran-2-yl) protecting group. Some loss is certainly due to on-column decomposition during silica-gel chromatography.

The propargylic OH function clearly needs protection. Absence of the silyl group in **2a** caused the intended ene reaction to produce, at room temperature, mainly untractible polar materials containing only small amounts (*ca.* 3%) of the desired carbocycle. The conversion **2a** → **3a** was accompanied by a side reaction generating dimer **9** as an unspecified mixture of diastereoisomers. This type of cross coupling has previously been exploited in a synthetically useful manner [12]. It presumably arises *via* a sequence involving oxidative addition of Pd^{2+} into the C–H bond of the terminal acetylene, followed by PdH_2 insertion and reductive elimination [13]. Formation of **9** could not be suppressed by changes in the catalyst system. It was, however, kept below 20% by working in dilute (0.005M) solution at room temperature. Replacement of the silyl by an acetyl protecting group in **2a** avoided the formation of **9**, but the cyclization was less clean and produced a lower overall yield (40%) of the corresponding acetylated cyclopentane derivative.

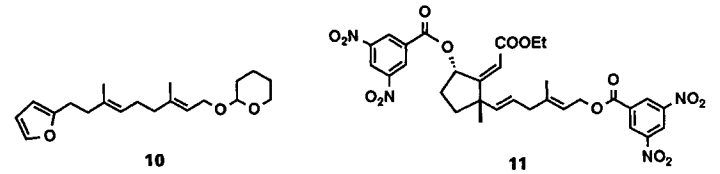


7a R = H
b R = CH_3

8



9



10 **11**

Curiously, **2b** failed to cyclize under the examined set of conditions. The $Pd(OAc)_2$/Ph_3P catalyst left the starting material unchanged even after 24 h at 60°. Prolonged heating to 80° produced a complex mixture containing only small amounts of the desired **3b**, that could not be obtained in pure form. The presence of Et_3N in the reaction mixture was ineffective at room temperature and destructive at > 60°. Nor did the employment of $PdCl_2(CH_3CN)_2$ or $Pd(dba)_2$ produce any isolable cyclopentane **3b**.

Extension of this cyclization to substrates other than 1,6-enynes met with little success. Neither the 1,6-dienyl alcohol **8** nor the enynones **7a**,**b** reacted in the desired manner. Nearly quantitative amounts of starting material were usually recovered from

reactions involving **8**. Similar failures have been reported for *Lewis*-acid-mediated ene cyclizations of 1,6-dienes [14]. On the other hand, complex mixtures were obtained from **7a**, while **7b** cyclized to furan **10** in 40% yield. Although undesired in the present context, this side reaction has previously been reported as a useful synthetic method to convert monofunctional aroylacetylenes into 2-arylfurans [15].

The cyclopentane derivatives **3** were obtained as viscous oils of limited stability. Their formation involves the generation of an additional stereocenter at the five-membered ring and of two new C=C bonds, so that a number of possible diastereoisomers may be anticipated. However, with the exception of **3a** and **3f**, the cyclopentanes appeared to be chromatographically and spectroscopically homogenous, even though they are necessarily mixtures of diastereoisomers due to the stereogenic nature of the THP protecting group. Compound **3a** was recognized as a *ca.* 2:1 mixture of isomers by the presence of a second set of signals in the ^{1}H-NMR spectrum. Amide **3f**, on the other hand, was partially separable by column chromatography into two isomeric compounds, isolated in a 2:1 ratio. To avoid complications arising from the THP-group stereocenter, configurational assignments were not carried out at this stage, but rather inferred from the characterization of the corresponding deprotected alcohols **4** and **5**.

Table 2. *Removal of the Protecting Groups by* 2N *HCl*

Substrate	Conditions			Product	Yield [%]
	Solvent	Temp. [°]	Time [h]		
3a	EtOH	50	15	**4a**/**5a**	80
3c	EtOH	40	15	**4c**	61
3d	MeOH	25	12	**4i**	90
3e	EtOH	40	8	**4e**	31
3f[1])	MeOH	25	2	**4f**	87
3f[2])	MeOH	25	2	**5f**	71
3g	EtOH	25	48	**6j**	50
3h	MeOH	40	8	**6k**	42

[1]) (2α,5α)-Isomer.
[2]) (2α,5β)-Isomer.

Removal of the protecting groups was effected by dilute HCl in EtOH or MeOH (*Table 2*). Careful examination (GC) of the crude reaction mixtures revealed the presence of a single compound following deprotection of **3c**, **3d**, and **3e**. Two isomers **4a**/**5a**, present in a ratio of *ca.* 1:2, were isolated after the deprotection of **3a**. Amides **4f** and **5f** were obtained as pure isomers by individual deprotection of their already separated precursors **3f**. Somewhat surprisingly, the free alcohols corresponding to **3g** and **3h** could not be obtained, nor could their transient presence be detected by reaction monitoring using TLC. Spontaneous ring closure with elimination of H_2O produced furans **6j** and **6k**.

^{1}H-NMR Spectroscopy clearly established **4a**/**5a** and **4f**/**5f** each as pair of geometrical isomers across the five-membered ring rather than across one of the newly formed C=C bonds. The latter were generated with complete stereocontrol in all cases. Coupling constants near 16 Hz established (*E*)-configuration for the disubstituted chain C=C bond. Intensive nuclear *Overhauser* enhancements (15–20%) between the quaternary

Me group and the exocyclic methylidene H-atom confirm exclusive (*Z*)-configuration in all substituted cases. Unfortunately, transannular through-space contacts between the substituents at the stereogenic centers seem to be weak and varying within the series, resulting in consistently small, if any, nuclear *Overhauser* effects (1D experiments). Precedents in the literature for configurational assignments are not available, since this particular five-membered-ring substitution pattern has previously been observed only as part of an annelated or bridged system.

After a number of failures, we succeeded to crystallize the bis(3,5-dinitrobenzoate) **11** of diol **4c**. Crystals suitable for X-ray analysis were grown by slow evaporation of solvent from a MeCN solution.

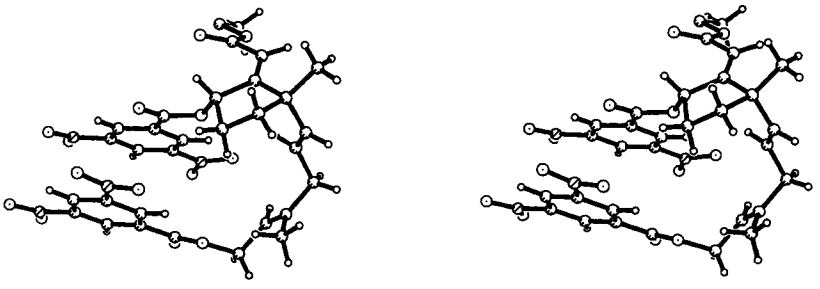


Fig. 1. *Stereoscopic representation of compound* **11**

In the crystal, the C_6 diene chain folds back upon the five-membered ring so as to allow a partial stacking of the two electron-poor aromatic rings (*Fig. 1*). This obviously overrides an unfavorable *endo* ring-chain 1,4-interaction resulting from a near synplanar alignment of the disubstituted chain C=C bond with one of the ring C–C bonds. Inspection of the crystal packing reveals that the molecules point towards each other with their aromatic rings. This results in the formation of layered stacks that are in tight *van-der-Waals* contacts with each other. No solvent is incorporated in the crystal lattice. The pucker of the cyclopentane ring represents an essentially strainless conformation. The quaternary Me group occupies a pseudo-equatorial position and is disposed *trans* to the aroylated ring OH substituent. This finding prompted a careful ^{1}H-NMR investigation of the parent ester **4c**. Complete assignments were carried out by H,H-COSY techniques in combination with 2D nuclear *Overhauser* (ROESY) spectroscopy (*Fig. 2*).

Again, no direct contacts between the stereogenic substituents are observed. However, one of the four ring CH_2 protons does share contacts to both the allylic ring H-atom

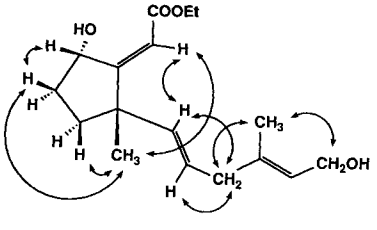


Fig. 2. *Selected NOE's for diol* **4c**

and the ring Me group. This clearly requires the three substituents to point into the same direction and constitutes an independent confirmation of the relative configuration in question.

With this information in hand, the configurational characterization of the whole series became feasible. Amide **4f** was recognized as the *cis*-(2α,5α)-isomer based on a similar relay of strong NOE's. This effect is not observed in the *trans*-(2α,5β)-isomer **5f**. Instead, a weak (2%) NOE appeared between the ring Me and OH groups. The chemical shifts (in $CDCl_3$) of **4f** and **5f** are almost identical with two exceptions. The quaternary Me group resonates 0.09 ppm downfield in **5f** and the resonances of the four ring CH_2 protons, nicely separated in **4f**, are partially overlapping and remain unassigned. By analogous argumentation **4a**, **4e**, and **4i** were assigned the relative *cis*-configuration. Additional evidence was gathered from weak but reproducible NOE's between the ring allylic H-atom and Me substituent (2%) of **4a** and between the former and the H-atoms of the disubstituted C=C bond ($\sim$4%) of **5a**. Because of the furan (**6j**, **k**) formation mentioned above, the NMR analysis was extended to include ketones **3g** and **3h**. A chemical-shift comparison of **3c**–**h** was undertaken with reference to the now assigned pair of isomers (2α,5α)- and (2α,5β)-**3f**. For the purpose of comparison, these compounds may be considered homogenous, since the THP-group stereocenter does not produce ^{1}H-NMR discernible epimers. Similar to the deprotected series, a characteristic downfield shift ($\Delta\delta \approx 0.15$ ppm) of the quaternary Me group together with an upfield shift ($\Delta\delta \approx 0.1$ ppm) of its geminal olefinic H-atom is observed for the *trans*-(2α,5β)-**3f** isomer. This is in contrast to all remaining compounds under comparison that have virtually identical shifts for these positions and are, therefore, assigned to be *cis*-isomers with respect to the ring Me and OH substituents.

All compounds shown represent racemic mixtures. Attempts to induce optical activity by the use of enantiomerically pure diphosphine ligands have been unavailing.

3. Discussion. – Based on the assignments above, we conclude that, except for **3a**, the predominantly or exclusively formed cyclopentane retains a *cis*-1,3-relationship between the ring OH substituent and the C_6 diene chain. This selectivity can be reconciled with the 'hydropalladation mechanism' suggested by *Trost* [8] for this type of ene reaction. This mechanism postulates an olefin insertion into a previously formed Pd–C σ-bond as the actual ring-forming step. The stereoelectronic constraints for such a process require an (ideally) parallel alignment of the Pd–C with the reacting C=C bond. Either face of this C=C bond is accessible for such an arrangement (*Fig. 3*). Approach from the *Si* side (*A*) enforces considerable proximity between the silyloxy and the COR substituents. This interaction is completely absent in the alternative conformation (*B*). Instead, a synperi-

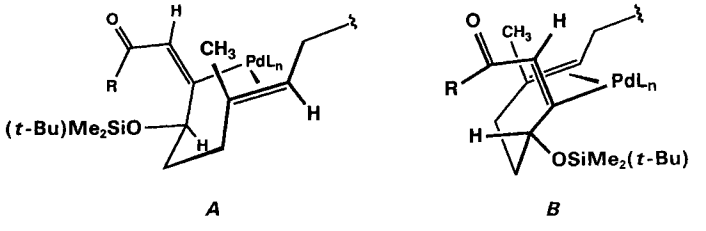


Fig. 3. *Hypothetical reaction intermediates*

clinal relationship between the silylated O-atom and the Pd-atom (including phosphine ligands) occurs. It appears to be sterically less demanding assuming olefin complexation by Pd within a square-planar coordination geometry. In the context of this model, the observed stereochemistry of the ene reaction is rationalized as the preferred formation of the sterically less encumbered intermediate (*B*). The lack of selectivity in the formation of **3a** is readily attributed to the absence of the decisive acetylenic substituent. However, no explanation is provided for the unselective cyclization of **2f**.

In both *A* and *B*, the O substituent occupies a pseudoequatorial position. An equivalent treatment of a set of analogous intermediates with a different chain pucker, resulting in a pseudoaxially disposed O-atom, leads to the same conclusion. Rationalization of the observed stereochemistry is not obvious within *Trost*'s alternative 'cyclopalladation mechanism' [8], that entails C–C bond formation from a π-Pd-enyne complex to yield a fused five-membered palladocycle containing σ-bonded Pd^{4+}. Considerable uncertainties as to the exact geometry of the enyne complexes virtually preclude an evaluation of their relevant conformations. Nor does inspection of the palladocycles reveal any distinguishing features. Even though both the hydropalladation and the cyclopalladation pathway represent hypothetical mechanisms, they did provide useful guidance for an explanation of our experimental results.

We are grateful to our colleagues from *Central Research* for conducting spectroscopic and combustion analyses. We wish to thank Dr. *G. Englert* and Dr. *W. Arnold* for their help with the NOE measurements and Prof. *E.-I. Negishi* for fruitful discussions. Particular appreciation is expressed to Dr. *Max Schmid* and Prof. *H.-J. Hansen* for their support of this project.

Experimental Part

We gratefully acknowledge the skilful technical assistance of *Christine Abrecht*

1. *General.* Commercially available reagents were used without further purification. THF was distilled under Ar from Na with benzophenone ketyl as indicator. Toluene was distilled from CaH_2. Reactions were monitored by TLC on 10 × 2.5 cm precoated silica *60F-254* plates (*E. Merck & Co.*). Chromatograms were developed in appropriate hexane/AcOEt mixtures and spots visualized with 4-methoxybenzaldehyde (4% in $EtOH/H_2SO_4$) stain at 150°. Column chromatography (silica *60*, 0.040–0.063 mm, *E. Merck & Co.*) refers to the procedure of *Still et al.* [16]. IR: *Nicolet 170-SX* FT-IR spectrometer; samples measured as thin films unless otherwise indicated; bands given in cm^{-1}. ^{1}H-NMR: *Bruker AC-250* or *Bruker AM-400*; samples measured in $CDCl_3$ (unless otherwise indicated) with TMS as internal standard; chemical shifts (δ) given in ppm, coupling constants (*J*) in Hz. EI-MS: *MS9*, updated with a *ZAB* console, *VG, Aldrincham*, UK; ionization energy 70 eV, ion source at 250°, *m/z* in % of the base peak. Abbreviations used for frequently observed mass fragments: DHP = dihydropyran, THP = tetrahydropyran-2-yl, THPOH = tetrahydropyran-2-ol.

2. Cyclization Substrates. 2.1. *(*RS,E,E*)-6,10-Dimethyl-12-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}dodeca-6,10-dien-1-yn-3-ol.* A 1.6M soln. of BuLi in hexane (87.2 ml, 140 mmol) was added slowly to a soln. of acetylene (3.9 g, 150 mmol) in THF (70 ml) at −75°. After 15 min, a soln. of *(*E,E*)-4,8-dimethyl-10-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}deca-4,8-dienal* (**1**. 13.3 g, 47.5 mmol) in THF (60 ml) was added dropwise. The mixture was left at −75° for 1 h, warmed to −30°, and kept at that temp. for another h. After purging with N_2, it was poured on ice-cold brine (*ca.* 1 l) and extracted three times with Et_2O. The combined extracts were washed with brine, dried (Na_2SO_4), filtered, and concentrated. FC on silica (500 g; hexane/AcOEt 4:1): 13.1 g (90%) of a colorless oil. IR: 3423*m*, 3306*m*, 2942*s*, 2854*s*, 2112*w*, 1666*w*, 1442*m*, 1384*m*, 1262*m*, 1200*m*, 1116*s*, 1074*s*, 1022*s*, 904*m*, 868*m*, 811*m*. ^{1}H-NMR (250 MHz): 5.34, 5.15 (2 br. *t*, $J \approx 7$, 2 C=CH); 4.64 (~ *t*, OCHO); 4.33 (*m*, C*H*OH); 4.27, 4.03 (2 br. *dd*,

J = 12, 7, C=CHCH_2O); 3.90, 3.52 (2*m*, pyran CH_2O); 2.45 (*d*, J = 2, C≡CH); 2.27–2.02 (*m*, 3 CH_2C=C); 1.90–1.46 (*m*, 4 CH_2); 1.66, 1.61 (2 *s*, 2 CH_3). MS: 222 (1, [M − DHP]$^+$), 204 (1, [M − THPOH]$^+$),188 (1), 186 (1), 171 (2), 161 (1), 145 (2), 137 (4), 119 (8), 109 (12), 91 (10), 85 (100).

2.2. *(*RS,E,E*)-3-{[(*tert*-Butyl)dimethylsilyl]oxy}-6,10-dimethyl-12-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}dodeca-6,10-dien-1-yne* (**2a**). A soln. of the preceding alcohol (15.3 g, 50 mmol) in CH_2Cl_2 (150 ml) was treated, at r.t., sequentially with (*t*-Bu)Me_2SiCl (9 g, 60 mmol) and DBU (9.12 g, 60 mmol). After 2 h, most of the solvent was removed and the residue diluted with hexane and washed exhaustively with H_2O. The hexane layer was dried ($MgSO_4$), filtered, and concentrated to a slightly yellow oil. FC on silica (500 g, hexane/AcOEt 95:5): 18.3 g (87%) of **2a** as a colorless oil. IR: 3310*m*, 2932*s*, 2856*s*, 2105*w*, 1668*w*, 1477*m*, 1385*m*, 1358*m*, 1254*s*, 1202*m*, 1095*s*, 1023*s*, 897*s*, 788*s*. ^{1}H-NMR (250 MHz): 5.40, 5.17 (2 br. *t*, $J \approx 7$, 2 C=CH); 4.63 (~ *t*, OCHO); 4.32 (*dt*, J = 2, 7, CHOSi); 4.26, 4.04 (2 br. *dd*, J = 12, 7.5, C=CHCH_2O); 3.91, 3.52 (2*m*, pyran CH_2O); 2.38 (*d*, J = 2, C≡CH); 2.18–2.0 (*m*, 3 C=CCH_2); 1.95–1.5 (*m*, 4 CH_2); 1.68, 1.60 (2*s*, 2 CH_3); 0.91 (*s*, *t*-Bu); 0.13, 0.11 (2*s*, 2 MeSi). MS: 336 (0.7, [M − DHP]$^+$), 261 (1, [M − THPOH and *t*-Bu]$^+$), 251 (2), 159 (14), 119 (14), 91 (18), 85 (100), 75 (26). Anal. calc. for $C_{25}H_{44}O_3Si$ (420.71): C 71.37, H 10,54; found: C 70.93, H 10.68.

2.3. *(*RS,E,E*)-7,11-Dimethyl-13-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}trideca-7,11-dien-2-yn-4-ol.* Prepared from propyne (18 g, 450 mmol) and **1** (28 g, 100 mmol) in the presence of BuLi (1.6M in hexane; 112.5 ml) as described in *2.1*. Purification by silica-gel chromatography (1.2 kg; hexane/AcOEt 4:1) furnished 20.2 g (63%) of a colorless oil. IR: 3426*m*, 2942*s*, 2871*s*, 2235*w*, 1672*w*, 1442*m*, 1384*m*, 1265*m*, 1200*m*, 1148*s*, 1119*s*, 1023*s*, 905*m*, 867*m*, 812*m*. ^{1}H-NMR (250 MHz): 5.55, 5,35 (2 br. *t*, $J \approx 7$, 2 C=CH); 4.71 (*m*, C*H*OH); 4.64 (~ *t*, OCHO); 4.24, 4.01 (2 br. *dd*, J = 12, 6.8, C=CHCH_2O); 3.89, 3.52 (2*m*, pyran CH_2O); 2.25–2.09 (*m*, 3 C=CCH_2); 1.98–1.49 (*m*, 4 CH_2); 1.87 (*d*, J = 2, CH_3C≡C); 1.74, 1.68 (2*s*, 2 CH_3). MS: 190 (0.5), 175 (2), 159 (2), 157 (2), 145 (3), 133 (2), 122 (8), 109 (6), 95 (12), 91 (10), 85 (100), 67 (42).

2.4. *(*RS,E,E*)-10{[(*tert*-Butyl)dimethylsilyl]oxy}-3,7-dimethyl-1-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}-trideca-2,6-dien-11-yne* (**2b**). By silylation of the preceding alcohol (2 g, 6.24 mmol) with (*t*-Bu)Me_2SiCl (1.12 g, 7.43 mmol) in the presence of DBU (1.13 g; 7.43 mmol) as described for **2a**. Chromatography on silica (100 g; hexane/AcOEt 95:5): 2.17 g (80%) of **2b** as a colorless oil. IR: 2931*s*, 2855*s*, 2230*w*, 1664*w*, 1465*m*, 1444*m*, 1360*m*, 1253*s*, 1200*m*, 1081*s*, 1024*s*, 837*s*, 777*s*. ^{1}H-NMR (250 MHz): 5.36, 5.13 (2 br. *t*, $J \approx 7$, 2 C=CH); 4.63 (~ *t*, OCHO); 4.28 (*m*, CHOSi); 4.26, 4.04 (2 br. *dd*, J = 12, 7.5, C=CHCH_2O); 3.91, 3.52 (2*m*, pyran CH_2O); 2.19–2.0 (*m*, 3 C=CCH_2); 1.82 (*d*, J = 2, CH_3≡C); 1.68, 1.61 (2*s*, 2 CH_3); 1.80–1.48 (*m*, 4 CH_2); 0.90 (*s*, *t*-Bu); 0.12, 0.09 (2*s*, 2 MeSi). MS: 349 (1, [M − THP]$^+$), 275 (2, [M − THPOH and *t*-Bu]$^+$), 265 (2), 207 (3), 183 (6), 159 (18), 133 (18), 105 (22), 97 (20), 85 (100), 75 (36).

2.5. *Ethyl (*RS,E,E*)-4-Hydroxy-7,11-dimethyl-13-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}trideca-7,11-dien-2-ynoate.* A soln. of ethyl propiolate (9.8 g, 100 mmol) in THF (200 ml) was cooled to −90°. BuLi (1.6M in hexane; 62.5 ml) was added dropwise, followed, after 30 min, by a soln. of **1** (28 g, 100 mmol) in THF (50 ml). After 1 h at −70°, the mixture was poured (without prior warming) on ice-cold brine and extracted three times with hexane. The combined extracts were washed with H_2O, dried (Na_2SO_4), filtered, and concentrated. Silica-gel chromatography (1 kg; hexane/AcOEt 4:1): 21.2 g (56%) of the title compound as a colorless oil. IR: 3408*s*, 2940*s*, 2855*s*, 2235*m*, 1712*s*, 1443*m*, 1385*m*, 1366*m*, 1248*s*, 1200*m*, 1117*m*, 1075*s*, 1022*s*, 904*m*, 866*m*, 812*m*, 751*m*. ^{1}H-NMR (250 MHz): 5.34, 5.16 (2 br. *t*, 2 C=CH); 4.65 (~ *t*, OCHO); 4.44 (*t*, J = 6.5, C*H*OH); 4.33–4.14, 4.07–3.98 (2*m*, CO_2CH_2, C=CHCH_2O); 3.90, 3.53 (2*m*, pyran CH_2O); 2.30–2.01 (*m*, 3 C=CCH_2); 1.95–1.50 (*m*, 4 CH_2); 1.65, 1.60 (2*s*, 2 CH_3); 1.32 (*t*, J = 7, $CO_2CH_2CH_3$). MS: 293 (1, [M − THP]$^+$), 277 (1, [M − THPO]$^+$), 185 (4), 181 (6), 166 (4), 163 (5), 135 (6), 117 (5), 93 (8), 85 (100).

2.6. *Ethyl (*RS,E,E*)-4-{[(*tert*-Butyl)dimethylsilyl]oxy}-7,11-dimethyl-13-{[(*RS*)-tetrahydro-2H-pyran-2-yl]oxy}trideca-7,11-dien-2-ynoate* (**2c**). Silylation of the preceding hydroxy ester (4.8 g, 12.7 mmol) with (*t*-Bu)Me_2SiCl (2 g, 13.3 mmol) as described for **2a**. Chromatography on silica (200 g; hexane/AcOEt 95:5) furnished 3.1 g (50%) of **2c** as a slightly yellow oil. IR: 2933*s*, 2857*s*, 2236*m*, 1716*s*, 1673*w*, 1468*m*, 1365*m*, 1246*s*, 1095*m*, 1023*m*, 838*m*, 779*m*. ^{1}H-NMR (250 MHz): 5.36, 5.14 (2 br. *t*, $J \approx 7$, 2 C=CH); 4.63 (~ *t*, OCHO); 4.43 (*t*, J = 6.5, CHOSi); 4.23 (*q*, J = 7, CO_2CH_2); 4.24, 4.02 (2 br. *dd* J = 12, 6.6, C=CHCH_2O); 3.90, 3.51 (2*m*, pyran CH_2O); 2.19–2.0 (*m*, 3 C=CCH_2); 1.89–1.47 (*m*, 4 CH_2); 1.68, 1.60 (2*s*, 2 CH_3); 1.31 (*t*, J = 7, $CO_2CH_2CH_3$); 0.91 (*s*, *t*-Bu); 0.15, 0.11 (2*s*, 2 MeSi). MS: 407 (0.5, [M − THP]$^+$), 333 (1.5, [M − THPOH and *t*-Bu]$^+$), 241 (4), 199 (4), 185 (6), 158 (12), 85 (100), 75 (26).

2.7. *8-{[(*tert*-Butyl)dimethylsilyl]oxy}octyl (*RS,E,E*)-4-Hydroxy-7,11-dimethyl-13-{[(*RS*)-tetrahydro-2H-pyran-2-yl]oxy}trideca-7,11-dien-2-ynoate.* A soln. of 8-{[(*tert*-butyl)dimethylsilyl]oxy}octyl propiolate (5 g, 16 mmol) in THF (70 ml) was treated, at −100°, with BuLi (1.6M in hexane, 10 ml), followed after 45 min by soln. of **1** (4 g, 14.3 mmol) in THF (10 ml). After 1 h at −100°, the soln. was warmed to −10° within another, then poured on ice-cold NH_4Cl soln. and extracted twice with hexane. The combined extracts were washed with H_2O, followed

by brine, dried ($MgSO_4$), filtered, and concentrated to a yellow oil (9.55 g). Chromatography on silica (500 g; hexane/AcOEt 95:5→9:1) yielded 7.1 g (84%) of the title compound as a slightly yellow oil. IR: 3400*m*, 2931*s*, 2856*s*, 2235*w*, 1714*s*, 1465*w*, 1388*w*, 1249*s*, 1097*m*, 1023*m*, 836*m*. ^{1}H-NMR (250 MHz): 5.29, 5.10 (2 br. *t*, 2 C=CH); 4.59 (*m*, OCHO); 4.38 (*m*, C*H*OH); 4.28–4.16, 4.04–3.91 (2 *m*, C=CHCH_2O); 4.11 (*t*, *J* = 6.5, CO_2CH_2); 3.90–3.78, 3.55–3.42 (2 *m*, pyran CH_2O); 3.55 (*t*, *J* = 6.5, CH_2OSi); 2.98 (*d*, *J* = 5, OH); 2.25–2.0 (*m*, 3 C=CCH_2); 1.64, 1.59 (2 *s*, 2 CH_3); 1.90–1.42 (*m*, 6 CH_2); 1.30 (*m*, 4 CH_2); 0.88 (*s*, *t*-Bu); 0.07 (*s*, 2 MeSi). MS: 491 (5, [*M* – THPO]$^+$), 313 (6), 278 (4), 261 (42), 85 (100).

2.8. *8-{[(*tert*-Butyl)dimethylsilyl]oxy}octyl (*RS,E,E*)-4-{[(*tert*-Butyl)dimethylsilyl]oxy}-7,11-dimethyl-13-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}trideca-7,11-dien-2-ynoate* (**2d**). Silylation of the preceding hydroxy ester (7 g, 11.8 mmol) with (*t*-Bu)Me_2SiCl (2.3 g; 15.3 mmol) in the presence of DBU (2.33 g; 15.3 mmol) was carried out as described for **2a**. Chromatography on silica (200 g; hexane/AcOEt 9:1): 7.3 g (87%) of **2d** as a slightly yellow oil. IR: 2931*s*, 2857*s*, 2230*w*, 1717*s*, 1673*w*, 1468*m*, 1386*m*, 1360*m*, 1251*s*, 1098*s*, 1024*s*, 837*s*, 778*s*. ^{1}H-NMR (250 MHz): 5.38, 5.15 (2 br. *t*, *J* ≈ 7, 2 C=CH); 4.63 (~ *t*, OCHO); 4.43 (*t*, *J* = 6.8, CHOSi); 4.34, 4.03 (2 br. *dd*, *J* = 12, 6.8, C=CHCH_2O); 4.16 (*t*, *J* = 6.7, CO_2CH_2); 3.91, 3.53 (2*m*, pyran CH_2O); 3.60 (*t*, *J* = 6.7, CH_2OSi); 2.19–1.99 (*m*, 3 C=CCH_2); 1.89–1.45 (*m*, 6 CH_2); 1.68, 1.60 (2*s*, 2 CH_3); 1.32 (*m*, 4 CH_2); 0.91, 0.90 (2*s*, 2 *t*-Bu); 0.15, 0.11, 0.05 (3*s*, 4 MeSi). MS: 621 (0.5, [*M* – THP]$^+$), 605 (0.5, [*M* – THPO]$^+$), 547 (3, [*M* – THPOH and *t*-Bu]$^+$), 479 (2), 415 (2), 310 (6), 287 (12), 213 (14), 185 (16), 159 (28), 85 (100). Anal. calc. for $C_{40}H_{74}O_6Si_2$ (707.20): C 67.94, H 10.55; found: C 67.74, H 10.85.

2.9. *Diethyl {(*RS,E,E*)-3-{[(*tert*-Butyl)dimethylsilyl]oxy}-6,10-dimethyl-12-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}dodeca-6,10-dien-1-ynyl} Phosphonate* (**2e**). BuLi (1.6M in hexane; 11 ml) was added dropwise to a soln. of **2a** (5 g, 11.9 mmol) in THF (40 ml) at –78°. Diethylchlorophosphate (2.42 g, 14 mmol) was introduced after 90 min and the resulting mixture kept at –78° for another h. After warming to –20°, it was poured on sat. NH_4Cl soln. and extracted twice with Et_2O. The combined extracts were washed with H_2O, dried (Na_2SO_4), and filtered. Solvent removal left a yellow oil, that was chromatographed on silica (400 g; hexane/AcOEt 8:2→7:3): 4.66 g (70%) of **2e** as a viscous oil. IR: 2932*s*, 2860*m*, 2195*m*, 1661*w*, 1470*m*, 1442*m*, 1263*m*, 1098*m*, 1026*s*, 976*m*, 836*m*, 776*m*. ^{1}H-NMR (250 MHz): 5.37, 5.14 (2 br. *t*, *J* ≈ 7, 2 C=CH); 4.66 (~ *t*, OCHO); 4.41 (*dt*, *J* = 3.4, 6.8, CHOSi); 4.31–3.96 (*m*, 3 CH_2O); 3.92, 3.51 (2*m*, pyran CH_2O); 2.20–2.0 (*m*, 3 C=CCH_2); 1.91–1.46 (*m*, 4 CH_2); 1.69, 1.60 (2*s*, 2 CH_3); 1.37 (*t*, *J* = 7.1; 2 $POCH_2CH_3$); 0.90 (*s*, *t*-Bu); 0.15, 0.11 (2*s*, 2 MeSi). MS: 499 (12, [*M* – (*t*-Bu)]$^+$), 471 (14, [*M* – THP]$^+$), 455 (8, [*M* – THPO]$^+$), 397 (24, [499 – THPOH]$^+$), 369 (34, [397 – C_2H_4]$^+$), 323 (24, [396 – EtOH]$^+$), 306 (72), 230 (76), 185 (90), 149 (42), 117 (74), 85 (100). Anal. calc. for $C_{29}H_{53}O_6PSi$ (556.80): C 62.56, H 9.59; found: C 61.98, H 9.83.

2.10. *(*RS,E,E*)-4-{[(*tert*-Butyl)dimethylsilyl]oxy}-N,N,7,11-tetramethyl-13-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}trideca-7,11-dien-2-ynamide* (**2f**). Compound **2a** (7.14 g, 17 mmol) was dissolved in THF (60 ml) and deprotonated at –78° with BuLi (1.6M in hexane; 14.8 ml). The resulting soln. was briefly warmed to –50°, recooled to –78°, and treated dropwise with dimethyl chlorocarbamate (2.56 g, 23.8 mmol). The mixture was allowed to reach 0° within 1 h, poured on ice-cold NH_4Cl soln. and extracted twice with hexane. The combined extracts were washed with H_2O, dried ($MgSO_4$), and concentrated to a yellow oil. It was chromatographed on silica (500 g; hexane/AcOEt 8:2→7:3): 7.9 g (94%) of **2f** as a pale yellow oil. IR: 2931*s*, 2856*m*, 2230*w*, 1644*s*, 1397*m*, 1257*m*, 1185*m*, 1094*s*, 1023*s*, 839*s*, 779*m*. ^{1}H-NMR (250 MHz): 5.37, 5.14 (2 br. *t*, *J* ≈ 7, 2 C=CH); 4.63 (~ *t*, OCHO); 4.47 (*t*, *J* = 6.3, CHOSi); 4.25, 4.02 (2 br. *dd*, *J* = 12, 6.8, C=CHCH_2O); 3.90, 3.51 (2*m*, pyran CH_2O); 3.20, 2.97 (2*s*, 2 NCH_3); 2.19–1.98 (*m*, 3 C=CCH_2); 1.87–1.45 (*m*, 4 CH_2); 1.68, 1.60 (2*s*, 2 CH_3); 0.90 (*s*, *t*-Bu); 0.13, 0.11 (2*s*, 2 MeSi). MS: 491 (2, M^+), 467 (2, [*M* – CH_3]$^+$), 434 (6, [*M* – (*t*-Bu)]$^+$), 406 (6, [*M* – THP]$^+$), 389 (4, [*M* – THPOH]$^+$), 322 (13), 258 (21), 240 (16), 198 (62), 190 (26), 185 (26), 165 (44), 159 (17), 124 (27), 85 (78), 72 (100).

2.11. *(*RS,E,E*)-9-{[(*tert*-Butyl)dimethylsilyl]oxy}-12,16-dimethyl-18-{[(*RS*)-tetrahydro-2*H*-pyran-2-yl]-oxy}octadeca-12,16-dien-7-yn-6-one* (**2g**). A soln. of **2a** (4.2 g, 10 mmol) in THF (30 ml) was treated dropwise with BuLi soln. (1.6M in hexane; 6.9 ml) at –78°. The mixture was transferred after 2 h *via* cannula into a soln. of caproic anhydride (2.35 g, 11 mmol) in Et_2O kept at –20°. The resulting soln. was allowed to reach r.t. within 1 h, poured into ice-cold $NaHCO_3$ soln., and extracted with hexane. The extracts were washed with H_2O, dried (Na_2SO_4), and concentrated to a yellowish oil (5.4 g). Chromatography on silica (500 g; hexane/AcOEt 97:3): 2.43 g (47%) **2g** as a colorless oil. IR: 2931*s*, 2857*m*, 2210*w*, 1679*s*, 1466*m*, 1360*m*, 1255*m*, 1097*s*, 1029*s*, 837*s*, 781*m*. ^{1}H-NMR (250 MHz): 5.37, 5.15 (2 br. *t*, *J* ≈ 7, 2 C=CH); 4.62 (~ *t*, OCHO); 4.46 (*t*, *J* = 6, CHOSi); 4.26, 4.02 (2 br. *dd*, *J* = 12, 7, C=CHCH_2O); 3.91, 3.51 (2*m*, pyran CH_2O); 2.54 (*t*, *J* = 7.3, $COCH_2$); 2.18–1.98 (*m*, 3 C=CCH_2); 1.88–1.46, 1.37–1.21 (2*m*, 7 CH_2); 1.68, 1.60 (2*s*, 2 CH_3); 0.91 (*s*, *t*-Bu); 0.90 (*m*, CH_3CH_2); 0.15, 0.11 (2*s*, 2 MeSi). MS: 359 (2.5, [*M* – THPOH and *t*-Bu]$^+$), 285 (5), 267 (4), 225 (10), 185 (6), 159 (8), 119 (6), 105 (7), 99 (16), 85 (100).

2.12. *(RS,2E,6E,21Z)-10-{[(tert-Butyl)dimethylsilyl]oxy}-3,7-dimethyl-1-{[(RS)-tetrahydro-2H-pyran-2-yl]oxy}triaconta-2,6,21-trien-11-yn-13-one* (**2h**). Prepared from **2a** (5.4 g, 12.8 mmol), BuLi (1.6M in hexane; 9.6 ml), and oleic anhydride (8.4 g, 15.4 mmol) as described in *2.11*. The crude dark yellow oil was chromatographed on silica (500 g; hexane/AcOEt 97:3): 6.2 g (70%) **2h** as a pale yellow oil. IR: 2927*s*, 2855*s*, 2215*m*, 1679*s*, 1464*m*, 1359*w*, 1254*m*, 1200*w*, 1093*s*, 1023*s*, 839*s*, 779*m*. ^{1}H-NMR (250 MHz): 5.34 (*m*, 3 C=CH); 5.14 (br. *t*, C=CH); 4.63 (~ *t*, OCHO); 4.46 (*t*, J = 6.5, CHOSi); 4.25, 4.02 (2 br. *dd*, J = 12, 7, C=CHCH_2O); 3.90, 3.51 (2*m*, pyran CH_2O); 2.54 (*t*, J = 7, $COCH_2$); 2.19–1.92, 1.43–1.90, 1.43–1.14 (3*m*, 20 CH_2); 1.68, 1.60 (2*s*, 2 CH_3); 0.91 (*s*, *t*-Bu); 0.88 (*m*, CH_3CH_2); 0.15, 0.11 (2*s*, 2 MeSi). MS: 583 (1, $[M - THPO]^+$), 525 (3, $[M$ – THPOH and *t*-Bu$]^+$), 451 (5, $[583 - Me_2(t\text{-Bu})SiOH]^+$), 185 (8), 167 (7), 159 (8), 85 (100).

2.13. *(E,E)-6,10-Dimethyl-12-{[(RS)-tetrahydro-2H-pyran-2-yl]oxy}dodeca-6,10-dien-1-yn-3-one* (**7a**). A soln. of the alcohol described in *2.1* (13.1 g, 42.7 mmol) in CH_2Cl_2 (50 ml) was added to a rapidly stirred suspension of MnO_2 (130 g) in CH_2Cl_2 (400 ml) at 0°. Stirring was continued for 4 h while warming to r.t. Solids were removed by filtration over compressed Na_2SO_4 and the concentrated filtrate was chromatographed on silica (500 g; hexane/AcOEt 4:1): 7.7 g (59%) of **7a** as a colorless oil. IR: 3250*m*, 2941*s*, 2871*s*, 2090*s*, 1683*s*, 1443*m*, 1385*m*, 1353*m*, 1200*m*, 1115*s*, 1077*m*, 1022*s*, 905*m*, 869*m*, 813*m*. ^{1}H-NMR (250 MHz): 5.35, 5.15 (2 br. *t*, $J \approx 7$, 2 C=CH); 4.63 (~ *t*, OCHO); 4.24, 4.02 (2 br. *dd*, J = 12, 7, C=CHCH_2O); 3.90, 3.51 (2*m*, pyran CH_2O); 3.23 (*s*, C≡CH); 2.69 (*t*, J = 7.5, $COCH_2$); 2.35 (*t*, J = 7.5, $COCH_2CH_2$); 2.19–2.00 (*m*, C=CCH_2CH_2C=C); 1.95–1.45 (*m*, 3 pyran CH_2); 1.67, 1.61 (2*s*, 2 CH_3). MS: 135 (10, $[C_9H_{11}O]^+$), 85 (100, $[THP]^+$). Anal. calc. for $C_{19}H_{28}O_3$ (304.43): C 74.96, H 9.27; found: C 74.54, H 9.46.

2.14. *(E,E)-7,11-Dimethyl-13-{[(RS)-tetrahydro-2H-pyran-2-yl]oxy}trideca-7,11-dien-2-yn-4-one* (**7b**). The alcohol described in *2.3* (1.6 g, 5 mmol) was oxidized with MnO_2 (16 g) as in the previous example. Silica-gel chromatography (100 g; hexane/AcOEt 95:5) afforded 0.96 g (60%) of **7b** as a colorless oil. IR: 2941*s*, 2869*s*, 2220*s*, 1674*s*, 1441*m*, 1387*m*, 1353*m*, 1283*w*, 1252*m*, 1163*m*, 1118*m*, 1076*m*, 1023*s*, 905*m*, 874*m*, 816*m*. ^{1}H-NMR (250 MHz): 5.37, 5.13 (2 br. *t*, $J \approx 7$, 2 C=CH); 4.63 (~ *t*, OCHO); 4.24, 4.02 (2 br. *dd*, J = 12, 7, C=CHCH_2O); 3.91, 3.50 (2*m*, pyran CH_2O); 2.62 (*t*, J = 8.3, $COCH_2$); 2.32 (br. *t*, $COCH_2CH_2$); 2.16–1.98 (*m*, C=CCH_2CH_2C=C); 2.03 (*s*, CH_3C≡C); 1.92–1.46 (*m*, 3 pyran CH_2); 1.67, 1.60 (2*s*, 2 CH_3). MS: 233 (3, $[M - THP]^+$), 134 (12), 123 (20), 107 (62), 85 (100), 67 (80).

2.15. *Ethyl (RS,E,E,E)-4-{[(tert-Butyl)dimethylsilyl]oxy}-7,11-dimethyl-13-{[(RS)-tetrahydro-2H-pyran-2-yl]oxy}trideca-2,7,11-trienoate* (**8**). A soln. of **1** (41 g, 146 mmol) and ethyl 3-nitropropionate (21.5 g; 146 mmol) in dry DMF was treated dropwise with DBU (22.5 g, 148 mmol). The resulting soln. was stirred overnight at r.t., then poured on ice-cold 2N HCl (~ 1.5 l), and extracted three times with a 1:1 mixture of hexane and Et_2O. The extracts were washed with H_2O followed by brine, dried (Na_2SO_4), and concentrated. Chromatography on silica (1.5 kg; hexane/AcOEt 4:1 containing 0.1% TEA): 27.3 g (50%) of a yellowish oil. A portion of this material (5.93 g, 15.6 mmol) was dissolved in pyridine together with (*t*-Bu)Me_2SiCl (2.7 g, 17.9 mmol). DBU (4.6 g, 30 mmol) had to be added to initiate the reaction. After 3 h at r.t., the mixture was poured on ice and extracted twice with hexane. The extracts were washed with H_2O, dried (Na_2SO_4), concentrated, and purified on silica (300 g; hexane/AcOEt 100:0→95:5): 7.41 g (96%) of **8** as a slightly yellow oil. IR: 2939*s*, 2958*s*, 1722*s*, 1659*m*, 1452*m*, 1366*m*, 1258*s*, 1196*s*, 1162*s*, 1118*s*, 1077*m*, 1025*s*, 977*m*, 837*s*, 776*m*. ^{1}H-NMR (250 MHz): 6.92 (*dd*, J = 15.5, 4.8, CH=CCO$_2$); 5.96 (*dd*, J = 15.5, 1.7, C=CHCO$_2$); 5.36, 5.11 (2 br. *t*, 2 C=C*H*CH$_2$); 4.63 (~ *t*, OCHO); 4.35–4.15 (*m*, CHOSi, CO_2CH_2); 4.20, 4.03 (2 br. *dd*, J = 12, 7, C=CHCH_2O); 3.90, 3.52 (2*m*, pyran CH_2O); 2.17–1.95 (*m*, 3 C=CHCH_2), 1.90–1.45 (*m*, 4 CH_2); 1.68, 1.58 (2*s*, 2 CH_3); 1.30 (*t*, J = 7.3, $CO_2CH_2CH_3$); 0.91 (*s*, *t*-Bu); 0.05, 0.03 (2*s*, 2 MeSi). MS: 409 (1, $[M - THP]^+$), 335 (3), 243 (9), 187 (8), 159 (10), 147 (16), 119 (32), 105 (8), 93 (14), 85 (100). Anal. calc. for $C_{28}H_{50}O_5Si$ (494.79): C 67.97, H 10.19; found: C 68.00, H 10.30.

3. Ene-Reactions. 3.1. *General Procedure.* Solid $Pd(OAc)_2$ (5 mol-%) together with Ph_3P (6 mol-%) were placed in a dried flask and put under Ar by three cycles of evacuation. Dry toluene (5 ml) was injected to dissolve the catalyst components. A soln. of the substrate **2**, dissolved in toluene, was introduced *via* cannula and the resulting mixture heated with stirring as indicated in *Table 1*. A positive pressure of Ar was maintained during that time, and samples for reaction monitoring were withdrawn with an Ar flushed syringe. In all cases, the product was found to move slightly faster on TLC in hexane/AcOEt mixtures. The completion of the reaction was usually accompanied by the precipitation of Pd black. After cooling, it was filtered off on *Celite*. The filtrate was concentrated and the residual crude material purified by FC on silica as indicated below. On-column decomposition clearly is a problem, as small-scale chromatography gave consistently better recoveries. All compounds **3** were obtained as moderately stable, viscous, colorless-to-pale-yellow oils that were freed of residual solvents by evacuation to 0.001 mbar for 48 h.

3.2. *(RS)-2-{{(E,E)-6-{3-{[(tert-Butyl)dimethylsilyl]oxy}-1-methyl-2-methylidenecyclopentyl}-3-methylhexa-2,5-dienyl}oxy}tetrahydro-2H-pyran* (**3a**). From **2a** (1.05 g, 2.5 mmol). Chromatography on silica (150 g,

hexane/AcOEt 98:2→95:5) separated 0.19 g of dimer **9** from 0.63 g of the less polar **3a**. IR: 3070*w*, 2955*s*, 2857*s*, 1668*w*, 1467*m*, 1359*m*, 1254*s*, 1200*m*, 1118*s*, 1024*s*, 973*m*, 879*m*, 836*s*, 776*s*. ^{1}H-NMR (250 MHz, major diastereoisomer): 5.46 (*d*, J = 15.3, C*H*=CHCH$_2$); 5.34 (*dt*, J = 15.3, 6.5, CH=C*H*CH$_2$); ~ 5.4 (partially obscured *t*, C=C*H*CH$_2$O); 5.10, 4.86 (2*m*, C=CH$_2$); 4.63 (~ *t*, OCHO); 4.45 (*m*, CHOSi); 4.24, 4.02 (2 br. *dd*, J = 12, 7, C=CHC*H*$_2$O); 3.90, 3.53 (2*m*, pyran CH$_2$O); 2.70 (br. *d*, J = 6.3, C=CCH$_2$C=C); 1.98–1.87 (*m*, 5 CH$_2$); 1.64 (*s*, CH$_3$); 1.19 (*s*, CH$_3$); 0.92 (*s*, *t*-Bu); 0.09, 0.07 (2*s*, 2 MeSi). MS: 405 (2, [M – CH$_3$]$^+$), 261 (15, [M – THPOH and *t*-Bu]$^+$), 193 (10), 187 (14), 159 (60), 131 (14), 93 (14), 85 (100), 75 (60).

3.3. *Ethyl* {(Z)-5α-{[(tert-*butyl*)*dimethylsilyl*]*oxy*}-2α-{(E,E)-4-*methyl*-6-{[(RS)-*tetrahydro*-2H-*pyran*-2-*yl*]*oxy*}*hexa*-1,4-*dienyl*}-2-*methylcyclopentylidene*}*acetate* (**3c**). From **2c** (1.05 g, 2.1 mmol) to yield, after chromatography (200 g; hexane/AcOEt 97:3), 0.7 g of **3c** as a colorless oil. IR: 2955*s*, 2855*s*, 1720*s*, 1661*w*, 1466*m*, 1371*m*, 1334*w*, 1299*w*, 1253*m*, 1199*s*, 1146*m*, 1117*m*, 1028*m*, 840*s*, 776*m*. ^{1}H-NMR (400 MHz): 5.58 (*s*, C=CHCO$_2$); 5.53 (*d*, J = 15.5, C*H*=CHCH$_2$); 5.44 (*m*, CHOSi); 5.41 (*dt*, J = 15.5, 7, CH=C*H*CH$_2$); ~ 5.38 (partially obscured *t*, C=C*H*CH$_2$O); 4.62 (~ *t*, OCHO); 4.23, 4.01 (2*m*, C=CHC*H*$_2$O); 4.14 (2*dq*, CO$_2$CH$_2$); 3.89, 3.52 (2*m*, pyran CH$_2$O); 2.71 (br. *d*, J = 6.8, C=CCH$_2$C=C); 2.06–1.97, 1.88–1.42 (2*m*, 5 CH$_2$); 1.64 (*s*, CH$_3$); 1.27 (*t*, J = 7, CO$_2$CH$_2$C*H*$_3$); 1.13 (*s*, CH$_3$); 0.82 (*s*, *t*-Bu); 0.11, 0.04 (2*s*, 2 MeSi). MS: 447 (1, [M – EtO]$^+$), 435 (2, [M – *t*-Bu]$^+$), 407 (1, [M – THP]$^+$), 391 (2, [M – THPO]$^+$), 333 (100, [M – THPOH and *t*-Bu]$^+$), 259 (38, [333 – CO and EtOH]$^+$), 231 (12), 198 (46), 185 (24), 171 (30), 159 (65), 85 (74), 75 (96). Anal. calc. for $C_{28}H_{48}O_5Si$ (492.77): C 68.25, H 9.82; found: C 68.58, H 10.35.

3.4. *8*-{[(tert-*Butyl*)*dimethylsilyl*]*oxy*}*octyl* {(Z)-5α-{[(tert-*Butyl*)*dimethylsilyl*]*oxy*}-2-*methyl*-2α-{(E,E)-4-*methyl*-6-{[(RS)-*tetrahydro*-2H-*pyran*-2-*yl*]*oxy*}*hexa*-1,4-*dienyl*}*cyclopentylidene*}*acetate* (**3d**). From **2d** (7.1 g, 10 mmol). The crude product was chromatographed on silica (250 g; hexane/AcOEt 98:2): 4.88 g (69%) of **3d** as a colorless oil. IR: 2931, 2858*s*, 1721*s*, 1660*w*, 1467*m*, 1387*m*, 1334*m*, 1298*w*, 1253*s*, 1198*s*, 1146*s*, 1099*s*, 1063*s*, 1024*s*, 836*s*, 776*s*. ^{1}H-NMR (250 MHz): 5.59 (*d*, J = 1.1, C=CHCO$_2$); 5.55 (*d*, J = 15.5, C*H*=CHCH$_2$); 5.42 (*dt*, J = 15.5, 6.5, CH=C*H*CH$_2$); ~ 5.45 (partially obscured *m*, C=C*H*CH$_2$O, CHOSi); 4.65 (~ *t*, OCHO); 4.26, 4.01 (2 br. *dd*, J = 12, 7, C=CHC*H*$_2$O); 4.08 (*t*, J = 6.7, CO$_2$CH$_2$); 3.91, 3.54 (2*m*, pyran CH$_2$O); 3.60 (*t*, J = 6.5, CH$_2$OSi); 2.72 (br. *d*, J = 7, C=CCH$_2$C=C); 2.10–1.97, 1.92–1.42, 1.42–1.23 (3*m*, 11 CH$_2$); 1.65, 1.13 (2*s*, 2 CH$_3$); 0.90, 0.83 (2*s*, 2 *t*-Bu); 0.12 (*s*, MeSi); 0.05 (*s*, 3 MeSi). MS: 691 (0.5, [M – CH$_3$]$^+$), 649 (2, [M – (*t*-Bu)]$^+$), 605 (2, [M – THPO]$^+$), 547 (68, [649 – THPOH]$^+$), 473 (6), 415 (10), 345 (8), 305 (12), 231 (60), 213 (44), 185 (24), 171 (48), 159 (78), 85 (80), 75 (100). Anal. calc. for $C_{40}H_{74}O_6Si_2$ (707.20): C 67.94, H 10.55; found: C 68.20, H 10.52.

3.5. *Diethyl* {{(Z)-5α-{[(tert-*Butyl*)*dimethylsilyl*]*oxy*}-2α-{(E,E)-4-*methyl*-6-{[(RS)-*tetrahydro*-2H-*pyran*-2-*yl*]*oxy*}*hexa*-1,4-*dienyl*}-2-*methylcyclopentylidene*}*methyl*} *Phosphonate* (**3e**). From **2e** (5.9 g, 10.6 mmol). Purification on silica (500 g; hexane/AcOEt 9:1→8:2) furnished 4 g of **3e** as a sligthly yellow oil. IR: 2955*s*, 2855*s*, 1640*w*, 1452*w*, 1388*w*, 1352*w*, 1250*s*, 1119*m*, 1055*s*, 1028*s*, 965*s*, 838*m*, 779*m*. ^{1}H-NMR (250 MHz): 5.56 (*d*, J = 16, C*H*=CHCH$_2$); 5.44 (partially obscured *dt*, CH=C*H*CH$_2$); 5.45–5.30 (*m*, CHOSi, C=C*H*CH$_2$O, C=CHP); 4.63 (~ *t*, OCHO); 4.26 and ~ 4.01 (2 br. *dd*, J = 12, 7, C=CHC*H*$_2$O); 4.13–3.95 (2*m*, 2 POCH$_2$); 3.91, 3.51 (2*m*, pyran CH$_2$O); 2.72 (br. *d*, J = 7, C=CCH$_2$C=C); 2.14–2.0, 1.91–1.44 (2*m*, 5 CH$_2$); 1.63, 1.14 (2*s*, 2 CH$_3$); 1.30, 1.27 (2*t*, J = 7, 2 POCH$_2$C*H*$_3$); 0.87 (*s*, *t*-Bu); 0.17, 0.13 (2*s*, 2 MeSi). MS: 541 (2, [M – CH$_3$]$^+$), 499 (100, [M – *t*-Bu]$^+$), 471 (12, [M – THP]$^+$), 455 (9, [M – THPO]$^+$), 397 (20, [499 – THPOH]$^+$), 369 (77, [397 – C$_2$H$_4$]$^+$), 323 (38, [369 – EtOH]$^+$), 185 (40). Anal. calc. for $C_{29}H_{53}O_6PSi$ (556.80): C 62.56, H 9.59; found: C 62.53, H 9.98.

3.6. {(Z)-5-{[(tert-*Butyl*)*dimethylsilyl*]*oxy*}-2α-{(E,E)-4-*methyl*-6-{[(RS)-*tetrahydro*-2H-*pyran*-2-*yl*]*oxy*}*hexa*-1,4-*dienyl*}-2-*methylcyclopentylidene*}-N,N-*dimethylacetamide* (**3f**). From **2f** (7.6 g, 15.5 mmol). Chromatography of the crude material on silica (500 g; hexane/AcOEt 8:2) furnished 0.35 g of the less polar (2α,5β)-isomer and 2.0 g of the more polar (2α,5α)-isomer together with 1.8 g of mixed fractions. The latter were rechromatographed (300 g silica, same eluent) to yield another 0.42 g of (2α,5β)-isomer and 0.46 g (2α,5α)-isomer together with 0.86 g of mixed fractions.

(2α,5β)-*Isomer:* IR: 2931*s*, 2855*s*, 1639*s*, 1467*m*, 1392*m*, 1253*m*, 1130*s*, 1056*s*, 1029*s*, 836*s*, 776*m*. ^{1}H-NMR (250 MHz): 5.74 (*d*, J = 1.5, C=CHCON); 5.49–5.32 (*m*, 3 C=CH); 5.11 (*m*, CHOSi); 4.61 (~ *t*, OCHO); 4.25, 4.01 (2 br. *dd*, J = 12, 7, C=CHC*H*$_2$O); 3.88, 3.50 (2*m*, pyran CH$_2$O); 2.93, 2.91 (2*s*, 2 NCH$_3$); 2.69 (br. *d*, C=CCH$_2$C=C); 1.94–1.45 (*m*, 5 CH$_2$); 1.62, 1.27 (2*s*, 2 CH$_3$); 0.83 (*s*, *t*-Bu); 0.05, 0.01 (2*s*, 2 MeSi). MS: 491 (0.5 M^+), 476 (3, [M – CH$_3$]$^+$), 434 (100, [M – *t*-Bu]$^+$), 406 (4, [M – THP]$^+$), 389 (4, [M – THPOH]$^+$), 350 (8, [434 – DHP]$^+$), 332 (4, [434 – THPOH]$^+$), 258 (11), 198 (96). Anal. calc. for $C_{28}H_{49}NO_4Si$: (491.79): C 68.38, H 10.04, N 2.85; found: C 68.54, H 10.35, N 2.84.

(2α,5α)-*Isomer:* IR: 2932*s*, 2855*s*, 1639*s*, 1465*m*, 1395*m*, 1253*m*, 1118*s*, 1023*s*, 837*s*, 777*m*. ^{1}H-NMR (250 MHz): 5.77 (*d*, J = 1.8, C=CHCON); 5.53 (*d*, J = 15.5, C*H*=CHCH$_2$); 5.42 (partially obscured *dt*, J = 15.5, 5.3, CH=C*H*CH$_2$); 5.37 (br. *t*, C=C*H*CH$_2$O); 5.13 (*m*, CHOSi); 4.61 (~ *t*, OCHO); 4.24, 3.99 (2 br. *dd*, J = 12, 7, C=CC*H*$_2$O); 3.88, 3.50 (2*m*, pyran CH$_2$O); 2.93, 2.91 (2*s*, 2 NCH$_3$); 2.71 (br. *d*, J = 6.3, C=CCH$_2$C=C); 1.93–1.37

(*m*, 5 CH_2); 1.63, 1.13 (2*s*, 2 CH_3); 0.82 (*s*, *t*-Bu); 0.04, 0.01 (2*s*, 2 MeSi). MS: same as for (2α,5β)-isomer. Anal. calc. for $C_{28}H_{49}NO_4Si$ (491.79): C 68.38, H 10.04, N 2.85; found: C 68.39, H 10.40, N 2.85.

3.7. *1-{(Z)-5α-{[(tert-Butyl)dimethylsilyl]oxy}-2α-{(E,E)-4-methyl-6-{[(RS)-tetrahydro-2H-pyran-2-yl]-oxy}hexa-1,4-dienyl}-2-methylcyclopentylidene}heptan-2-one* (**3g**). From **2g** (2.59 g, 5 mmol). Chromatography on silica (400 g; hexane/AcOEt 7:3) yielded 2.11 g of **3g** as colorless oil. IR: 2937*s*, 2856*m*, 1695*m*, 1632*m*, 1465*w*, 1252*m*, 1118*m*, 1054*s*, 1024*s*, 836*m*, 779*m*. ^{1}H-NMR (250 MHz): 5.93 (*d*, *J* = 1.4, C=CHCO); 5.54 (*d*, *J* = 16, C*H*=CHCH$_2$); 5.49–5.34 (*m*, CH=C*H*CH$_2$, C=C*H*CH$_2$O, CHOSi); 4.64 (~ *t*, OCHO); 4.26, 4.03 (2 br. *dd*, *J* = 12, 7, C=CHC*H*$_2$O); 3.90, 3.54 (2*m*, pyran CH$_2$O); 2.74 (*d*, *J* = 6.3, C=CCH$_2$C=C); 2.43 (*t*, *J* = 7.3, COC*H*$_2$CH$_2$); 2.05–1.21 (*m*, 8 CH$_2$); 1.66, 1.13 (2*s*, 2 CH$_3$); 0.89 (*m*, C*H*$_3$CH$_2$); 0.82 (*s*, *t*-Bu); 0.13, 0.04 (2*s*, 2 MeSi). MS: 503 (1.5, $[M - CH_3]^+$), 461 (1, $[M - t\text{-Bu}]^+$), 433 (1, $[M - THP]^+$), 416 (6, $[M - THPOH]^{+\cdot}$), 401 (3), 359 (22, $[416 - t\text{-Bu}]^+$), 349 (3), 323 (5), 317 (6), 285 (14, $[416 - Me_2Si(t\text{-Bu})O]^+$), 225 (100), 159 (24), 151 (14), 99 (8), 85 (60). Anal. calc. for $C_{31}H_{54}O_4Si$ (518.86): C 71.76, H 10.49; found: C 71.53, H 10.61.

3.8. *(Z)-1-{(Z)-5α-{[(tert-Butyl)dimethylsilyl]oxy}-2α-{(E,E)-4-methyl-6-{[(RS)-tetrahydro-2H-pyran-2-yl]oxy}hexa-1,4-dienyl}-2-methylcyclopentylidene}nonadec-10-en-2-one* (**3h**). From **2h** (6.1 g, 8.9 mmol). Chromatography on silica (400 g; hexane/AcOEt 98:2) yielded 2.2 g of **3h** as a pale yellow syrup. IR: 2926*s*, 2854*s*, 1694*m*, 1633*m*, 1462*m*, 1365*w*, 1252*m*, 1116*s*, 1056*s*, 1025*s*, 836*s*, 777*m*. ^{1}H-NMR (250 MHz): 5.92 (*d*, *J* = 1.4, C=CHCO); 5.58–5.27 (*m*, 5 olefin. H, CHOSi); 4.61 (~ *t*, OCHO); 4.26, 4.02 (2 br. *dd*, CH=CHC*H*$_2$O); 3.90, 3.53 (2*m*, pyran CH$_2$O); 2.73 (br. *d*, *J* = 7, C=CCH$_2$C=C); 2.42 (*t*, *J* = 7, COC*H*$_2$CH$_2$); 2.09–1.17 (*m*, 18 CH$_2$); 1.65, 1.12 (2*s*, 2 CH$_3$); 0.88 (*m*, C*H*$_3$CH$_2$); 0.82 (*s*, *t*-Bu); 0.11, 0.04 (2*s*, 2 MeSi). MS: 684 (0.5, $M^{+\cdot}$), 669 (10, $[M - CH_3]^+$), 627 (3, $[M - t\text{-Bu})]^+$), 599 (4, $[M - THP]^+$), 582 (20, $[M - THPOH]^{+\cdot}$), 567 (7, $[582 - CH_3]^+$), 525 (40, $[582 - t\text{-Bu})]^+$), 489 (24), 451 (20), 391 (37), 317 (26), 159 (42), 85 (92), 72 (100).

4. Removal of the Protecting Groups. 4.1. *General Procedure*. The protected cyclopentane **3** was dissolved in alcohol (~ 1 mmol/10 ml). 2N HCl (0.15 equiv.) was added dropwise and the reaction mixture treated as indicated in *Table 2*. After cooling, it was poured into ice-cold brine containing 10% $NaHCO_3$ soln. and extracted with Et_2O. The combined extracts were washed with H_2O, followed by brine, and dried (Na_2SO_4). The crude material was purified by FC on silica using the eluents indicated below. Appropriate fractions were concentrated, filtered, and finally pumped dry at 0.001 mbar for 48 h. The pure products **4**, **5**, or **6** were obtained as viscous oils.

4.2. *3α-[(E,E)-6-Hydroxy-4-methylhexa-1,4-dienyl]-3-methyl-2-methylidenecyclopentan-1α-ol* (**4a**) *and 3α-[(E,E)-6-Hydroxy-4-methylhexa-1,4-dienyl]-3-methyl-2-methylidenecyclopentan-1β-ol* (**5a**). From **3a** (0.62 g, 1.47 mmol). Chromatography of the crude product (100 g silica; hexane/AcOEt 3:1) furnished 104 mg of **5a** and 13 mg of the slightly more polar **4a** together with 145 mg of mixed fractions.

Data of **5a**: IR: 3334*s*, 3076*w*, 3021*w*, 2959*s*, 2868*s*, 1661*w*, 1651*w*, 1443*m*, 1382*w*, 1326*w*, 1074*m*, 1004*s*, 973*s*, 905*m*. ^{1}H-NMR (400 MHz, (D$_6$)DMSO): 5.45 (*d*, *J* = 15.5, C*H*=CHCH$_2$); 5.27 (*dt*, *J* = 15.5, 7, CH=C*H*CH$_2$); 5.25 (partially obscured *t*, C=C*H*CH$_2$O); 5.08, 4.80 (2*m*, C=CH$_2$); 4.91 (*d*, *J* = 5.6, CHO*H*); 4.47 (*t*, *J* = 5.2, CH$_2$O*H*); 4.27 (*m*, C*H*OH); 3.92 (~ *t*, *J* ≈ 6, CH$_2$O); 2.62 (br. *d*, *J* = 7.2, C=CCH$_2$C=C); 1.89–1.80, 1.60–1.40 (2*m*, 2 ring CH$_2$); 1.53, 1.14 (2*s*, 2 CH$_3$). MS: 207 (14, $[M - CH_3]^+$), 204 (3, $[M - H_2O]^{+\cdot}$), 189 (10, $[207 - H_2O]^+$), 171 (8), 145 (15), 134 (22), 119 (80), 105 (53), 95 (48), 93 (100), 91 (76).

Data of **4a**: IR: 3328*s*, 3075*w*, 3024*w*, 2959*s*, 2928*s*, 2866*m*, 1670*w*, 1655*w*, 1448*m*, 1382*w*, 1327*w*, 1077*m*, 999*s*, 974*s*, 899*m*. ^{1}H-NMR (400 MHz, (D$_6$)DMSO): 5.48 (*d*, *J* = 15.6, C*H*=CHCH$_2$); 5.35–5.25 (*m*, CH=C*H*CH$_2$, C=C*H*CH$_2$O); 5.10, 4.79 (2*m*, C=CH$_2$); 4.90 (*d*, *J* = 5.3, CHO*H*); 4.48 (*t*, *J* = 5.2, CH$_2$O*H*); 4.32 (*m*, C*H*OH); 3.93 (~ *t*, *J* ≈ 5.4, CH$_2$O); 2.64 (br. *d*, *J* = 6.8, C=CCH$_2$C=C); 1.87–1.78, 1.75–1.67 (2*m*, ring CH$_2$); 1.54, 1.10 (2*s*, 2 CH$_3$); 1.48–1.33 (*m*, 2 ring CH$_2$). MS: same as for **5a**.

4.3. *Ethyl {(Z)-5α-Hydroxy-2α-[(E,E)-6-hydroxy-4-methylhexa-1,4-dienyl]-2-methylcyclopentylidene}-acetate* (**4c**). From **3c** (0.63 g, 1.28 mmol). Chromatography (60 g silica; hexane/AcOEt 3:1): 0.23 g, of **4c** as a colorless oil. IR: 3427*m*, 2963*m*, 2869*m*, 1691*s*, 1645*m*, 1446*w*, 1371*m*, 1344*m*, 1301*m*, 1209*s*, 1154*w*, 1088*w*, 1027*m*, 973*m*. ^{1}H-NMR (400 MHz): 5.74 (*d*, *J* = 1.8, C=CHCO$_2$); 5.46 (*d*, *J* = 15.6, C*H*=CHCH$_2$); 5.42 (partially obscured *t*, C=C*H*CH$_2$O); 5.39 (*dt*, *J* = 15.6, 6.4, CH=C*H*CH$_2$); 4.94 (*m*, C*H*OH); 4.84 (*d*, *J* = 2.3, CHO*H*); 4.21 (*q*, *J* = 7.1, CO$_2$CH$_2$); 4.15 (*d*, *J* = 6.9, CH$_2$OH); 2.71 (*d*, *J* = 6.3, C=CCH$_2$C=C); 2.10 (*ddt*, *J* = 12.5, 4.6, 7.2, H$_\beta$–C(4)); 1.90 (*ddd*, *J* = 11.8, 6.6, 4.6, H$_\alpha$–C(3)); 1.81 (*ddt*, *J* = 12.5, 9.5, 6.6, H$_\alpha$–C(4)); 1.64 (*s*, CH$_3$); 1.46 (*ddd*, *J* = 11.8, 9.5, 7.2, H$_\beta$–C(3)); 1.32 (*t*, *J* = 7.1, CO$_2$CH$_2$C*H*$_3$); 1.18 (*s*, CH$_3$). MS: 276 (4, $[M - H_2O]^{+\cdot}$), 230 (34, $[276 - EtOH]^{+\cdot}$), 179 (42), 134 (54), 119 (70), 105 (56), 95 (100). Anal. calc. for $C_{17}H_{26}O_4$ (294.39): C 69.36, H 8.90; found: C 69.11, H 9.07.

4.4. *Diethyl {{(Z)-5α-Hydroxy-2α-[(E,E)-6-hydroxy-4-methylhexa-1,4-dienyl]-2-methylcyclopentylidene}-methyl} Phosphonate* (**4e**). From **3e** (0.41 g, 0.74 mmol). Chromatography on silica (20 g; hexane/AcOEt 1:1): 82 mg of **4e** as a pale yellow oil. IR: 3392*s*, 2935*s*, 2869*m*, 1671*w*, 1629*m*, 1445*m*, 1392*m*, 1292*w*, 1214*s*, 1164*m*, 1025*s*,

972*s*, 827*m*. ^{1}H-NMR (250 MHz): 5.65 (br. *s*, CHO*H*); 5.51–5.33 (*m*, 4 olef. H); 4.87 (*m*, C*H*OH); 4.15 (*d*, *J* = 7.5, C*H*$_2$OH); 4.08 (*m*, 2 POCH$_2$); 2.71 (br. *d*, *J* = 5.8, C=CCH$_2$C=C); 2.16–2.02, 1.95–1.66, 1.55–1.44 (3*m*, 2 ring CH$_2$); 1.64 (*s*, CH$_3$); 1.34, 1.33 (2*t*, *J* = 7.3, 2 POCH$_2$C*H*$_3$); 1.17 (*s*, CH$_3$). MS: 341 (5, $[M - OH]^+$), 340 (2, $[M - H_2O]^+$), 325 (4, $[340 - CH_3]^+$), 311 (8, $[340 - C_2H_5]^+$), 297 (3), 295 (3), 283 (6), 273 (5), 261 (76, $[325 - H_2O$ and EtOH$]^+$), 243 (24), 230 (25), 145 (25), 131 (48), 117 (48), 105 (64), 91 (100).

4.5. {(Z)-5α-*Hydroxy-2α-[(*E,E*)-6-hydroxy-4-methylhexa-1,4-dienyl]-2-methylcyclopentylidene*}-N,N-*dimethylacetamide* (**4f**). From (2α,5α)-**3f** (1.78 g, 3.62 mmol). Chromatography (100 g of silica; hexane/AcOEt 1:1→1:4): 0.93 g of **4f** as a pale yellow oil. IR: 3404*s*, 2942*s*, 2868*m*, 1651*m*, 1601*s*, 1495*w*, 1449*w*, 1397*m*, 1309*w*, 1260*w*, 1172*w*, 1144*w*, 1085*w*, 1057*w*, 1023*m*, 974*m*. ^{1}H-NMR (400 MHz, (D$_6$)DMSO): 6,06 (*d*, *J* = 1.7, C=CHCON); 5.78 (*d*, *J* = 1.6, CHO*H*); 5.50 (*d*, *J* = 15.6, C*H*=CHCH$_2$); 5.36 (*dt*, *J* = 15.6, 6.8, CH=C*H*CH$_2$); 5.29 (br. *t*, *J* ≈ 7, C=C*H*CH$_2$O); 4.67 (br. *t*, C*H*OH); 4.48 (*t*, *J* = 5.2, CH$_2$O*H*); 3.93 (~ *t*, *J* ≈ 5.6, C*H*$_2$OH); 3.03, 2.89 (2*s*, 2 NCH$_3$); 2.66 (br. *d*, *J* = 6.8, C=CCH$_2$C=C); 1.95–1.86, 1.84–1.77, 1.63–1.54, 1.46–1.38 (4*m*, 2 ring CH$_2$); 1.55, 1.15 (2*s*, 2 CH$_3$). MS: 293 (1, M^+), 276 (4, $[M - OH]^+$), 275 (4, $[M - H_2O]^+$), 262 (1), 260 (1), 258 (2), 246 (3), 232 (2), 230 (3), 208 (8), 196 (48), 178 (22), 155 (24), 141 (32), 119 (22), 105 (22), 93 (22), 91 (38), 72 (100). Anal. calc. for $C_{17}H_{27}NO_3$ (293.41): C 69.59, H 9.28, N 4.77; found: C 69.57, H 9.21, N 4.63.

4.6. {(Z)-5β-*Hydroxy-2α-[(*E,E*)-6-hydroxy-4-methylhexa-1,4-dienyl]-2-methylcyclopentylidene*}-N,N-*dimethylacetamide* (**5f**). From (2α,5β)-**3f** (0.67 g, 1.36 mmol). Chromatography on silica (20 g; hexane/AcOEt 1:1→1:9): 284 mg of **5f**. IR: 3401*s*, 2932*s*, 2873*s*, 1651*m*, 1600*s*, 1496*m*, 1448*w*, 1397*m*, 1304*w*, 1259*w*, 1176*w*, 1145*w*, 1014*m*, 979*m*, 866*w*. ^{1}H-NMR (400 MHz, (D$_6$)DMSO): 6.07 (*d*, *J* = 1.6, C=CHCON); 5.88 (*d*, *J* = 1.6, CHO*H*); 5.45 (*d*, *J* = 15.6, C*H*=CHCH$_2$); 5.33 (*dt*, *J* = 15.6, 6.8, CH=C*H*CH$_2$); 5.27 (br. *t*, *J* ≈ 7, C=C*H*CH$_2$O); 4.64 (*m*, C*H*OH); 4.47 (*t*, *J* = 5.6, CH$_2$O*H*); 3.92 (~ *t*, *J* = 5.6, C*H*$_2$OH); 3.02, 2.89 (2 *s*, 2 NCH$_3$); 2.65 (br. *d*, *J* = 6.8, C=CCH$_2$C=C); 1.92–1.83, 1.71–1.58 (2 *m*, 2 ring CH$_2$); 1.55, 1.21 (2 *s*, 2 CH$_3$). MS: same as for **4f**.

4.7. *8-Hydroxyoctyl* {(Z)-5α-*Hydroxy-2α-[(*E,E*)-6-hydroxy-4-methylhexa-1,4-dienyl]-2-methylcyclopentylidene*}*acetate* (**4i**). From **3d** (0.2 g, 0.28 mmol). Chromatography on silica (20 g; hexane/AcOEt 6:4→1:1): 100 mg of **4i** as a colorless oil. IR: 3400*s*, 2931*s*, 2859*m*, 1690*s*, 1645*m*, 1461*w*, 1389*w*, 1346*m*, 1300*w*, 1208*s*, 1155*w*, 1062*m*, 1010*m*. ^{1}H-NMR (250 MHz): 5.74 (*d*, *J* = 1.7, C=CHCO); 5.50–5.32 (*m*, 3 olef. H); 4.96 (*m*, C*H*OH); 4.88 (*d*, *J* = 2, CHO*H*); 4.14 (*m*, CO$_2$CH$_2$, C=CHC*H*$_2$O); 3.64 (~ *t*, CH$_2$C*H*$_2$OH); 2.71 (br. *d*, *J* ≈ 7, C=CCH$_2$C=C); 2.18–2.03, 1.96–1.29 (2 *m*, 8 CH$_2$); 1.65, 1.19 (2 *s*, 2 CH$_3$). MS: 376 (2, $[M - H_2O]^+$), 358 (2, $[M - 2\,H_2O]^+$), 283 (3, $[M - C_7H_{11}O]^+$), 248 (4, $[M - HO(CH_2)_8OH]^+$), 230 (26, $[248 - H_2O]^+$), 151 (56), 147 (48), 134 (64), 119 (56), 105 (50), 95 (88), 93 (62), 91 (48), 81 (58).

4.8. (RS,E,E)-6-[*5,6-Dihydro-4-methyl-2-pentyl-4*H-*cyclopenta*[b]*furan-4-yl*]-*3-methylhexa-2,5-dien-1-ol* (**6j**). From **3g** (2.1 g, 4.05 mmol). Chromatography on silica (150 g; hexane/AcOEt 9:1→8:2): 0.62 g of **6j**. IR: 3346*m*, 2930*s*, 2859*s*, 1724*w*, 1671*w*, 1633*w*, 1556*w*, 1452*m*, 1378*w*, 1315*w*, 1232*m*, 1150*w*, 1089*w*, 1000*m*, 973*s*, 931*w*, 797*w*. ^{1}H-NMR (250 MHz): 5.81 (*s*, furan H); 5.61 (*d*, *J* = 15.5, C*H*=CHCH$_2$); 5.40 (br. *t*, C=C*H*CH$_2$O); 5.28 (*dt*, *J* = 15.5, 7, CH=C*H*CH$_2$); 4.15 (*d*, *J* = 7, C*H*$_2$OH); 2.68 (br. *d*, *J* ≈ 7, C=CCH$_2$C=C); 2.66, 2.57 (2*t*, *J* = 7.7, 2 C=C(O)CH$_2$); 2.34, 2.20 (2*dt*, *J* = 11, 5.5, ring CH$_2$); ~ 1.6 (partially obscured *m*, CH$_2$); 1.42–1.27 (*m*, 2 CH$_2$); 1.64, 1.26 (2*s*, 2 CH$_3$); 0.90 (*m*, C*H*$_3$CH$_2$). MS: 302 (45, M^+), 287 (100, $[M - CH_3]^+$), 217 (86, $[M - C_5H_9O]^+$), 159 (22), 151 (30), 145 (20), 131 (18), 119 (22), 105 (35), 91 (38).

4.9. (RS,E,E)-6-{*2-[(Z)-Heptadec-8-enyl]-5,6-dihydro-4-methyl-4*H-*cyclopenta*[b]*furan-4-yl*}-*3-methylhexa-2,5-dien-1-ol* (**6k**). From **3h** (0.55 g, 0.8 mmol). Chromatography on silica (70 g; hexane/AcOEt 95:5): 156 mg of **6k** as a pale yellow oil. IR: 3321*m*, 3004*w*, 2925*s*, 2854*s*, 1672*w*, 1634*w*, 1556*m*, 1480*m*, 1374*w*, 1343*w*, 1311*w*, 1292*m*, 1000*m*, 972*m*, 797*w*. ^{1}H-NMR (250 MHz): 5.80 (*s*, furan H); 5.62 (*d*, *J* = 15.5, *trans* C*H*=CHCH$_2$); 5.42 (br. *t*, C=C*H*CH$_2$O); 5.34 (*m*, *cis* C*H*=C*H*); 5.30 (*dt*, *J* = 15.5, 7, *trans* CH=C*H*CH$_2$); 4.16 (br. *d*, *J* ≈ 6, C*H*$_2$OH); 2.68 (*d*, *J* ≈ 7, C=CCH$_2$C=C); 2.66, 2.57 (2*t*, *J* = 7.3, 2 C=C(O)CH$_2$); 2.34, 2.21 (2*dt*, *J* = 11, 5.5, ring CH$_2$); 2.06–1.93 (*m*, 2 C=CCH$_2$); 1.66–1.53, 1.42–1.20 (2*m*, 11 CH$_2$); 1.64, 1.25 (2*s*, 2 CH$_3$); 0.88 (*m*, C*H*$_3$CH$_2$). MS: 468 (34, M^+), 453 (100, $[M - CH_3]^+$), 437 (6), 383 (42), 370 (8), 357 (8), 317 (8), 159 (18), 145 (32), 105 (22). Anal. calc. for $C_{32}H_{52}O_2$ (486.78): C 81.99, H 11.18; found: C 81.39, H 11.43.

5. Compound 11. – 5.1. (E,E)-6-{*3α-[(3,5-Dinitrobenzoyl)oxy]-2-[(*Z*)-(ethoxycarbonyl)methylidene]-1β-methylcyclopentyl*}-*3-methylhexa-2,5-dienyl 3,5-Dinitrobenzoate* (**11**). Diol **4c** (200 mg, 0.678 mmol) was dissolved in MeCN (10 ml). Et$_3$N (0.368 ml, 2.72 mmol) followed by 3,5-dinitrobenzoyl chloride (627 mg, 2.72 mmol) was introduced at 0°, and the resulting soln. was stirred overnight at r.t. Then, it was diluted with ice-cold brine and extracted twice with AcOEt. The combined extracts were washed with H$_2$O and brine, dried (Na$_2$SO$_4$), filtered, and concentrated to a brown oil. Chromatography on silica (90 g; hexane/AcOEt 9:1→4:1) produced a yellow oil that spontaneously crystallized. Yield: 374 mg (81%). M.p. 110.6–112°. IR (KBr): 3082*m*, 2935*w*, 1730*s*, 1626*m*, 1547*s*, 1461*w*, 1345*s*, 1275*s*, 1202*m*, 1165*m*, 1081*w*, 1030*w*, 973*w*, 926*w*, 725*m*. ^{1}H-NMR (250 MHz): 9.22, 9.19 (2*t*, *J* = 2.2, 2 arom. H); 9.15, 9.09 (2*d*, *J* = 2.2, 4 arom. H); 6.48 (*m*, CO$_2$CH); 5.92 (*d*, *J* = 1.6, C=CHCO$_2$); 5.70–5.47

(*m*, 3 olef. H); 4.96 (*d*, $J = 7$, C=CHCH_2O); 4.03 (*m*, $CO_2CH_2CH_3$); 2.91 (br. *d*, $J = 7$, C=CCH_2C=C); 2.45–2.30, 2.10–1.80, 1.72–1.58 (3 *m*, 2 ring CH_2); 1.81, 1.30 (2 *s*, 2 CH_3); 1.17 (*t*, $J = 7$, $CO_2CH_2CH_3$). MS: 470 (8, $[M - (\text{dinitrobenzoic acid})]^{+\cdot}$), 425 (2), 403 (6), 258 (18, $[M - 2\,(\text{dinitrobenzoic acid})]^{+\cdot}$), 195 (100), 185 (58), 149 (64), 119 (36), 105 (42), 93 (68), 91 (56), 75 (82).

5.2. *X-Ray Analysis of* **11**. *Crystal Data:* Crystals were grown by slow evaporation of MeCN at r.t. Space group triclinic $P\bar{1}$; cell dimensions: $a = 10.400(2)$, $b = 11.009(3)$, $c = 15.338(3)$ Å; $\alpha = 100.69(2)°$, $\beta = 108.43(2)°$, $\gamma = 98.95(2)°$, $D = 1.42$ Mg/m^3, $Z = 2$; $\mu(\text{MoK}\alpha) = 0.11$ mm^{-1}. *Data Collection:* Data were collected on a *Nicolet R3m* four-circle diffractometer fitted with a *LT1* cooling apparatus. Temp. 190 K; wavelength: 0.71069 Å; scan mode $\Theta/2\Theta$; scan speed 3.3°/min minimum speed; strong reflections measured up to 10°/min; scan width 1.8°; 2Θ range 0–50°; peak: background ratio 5:1, total data measured: 5996 excluding standards; total observed: 3875; rejection criterion $I > 2.5\sigma(I)$; number of parameters: 441; weights $w = 1/\sigma(F)+0.001|F|^2$.

Structure Determination and Refinement: The structure was determined by direct methods using the *Nicolet* SHELXTL PLUS (*MicroVAX II*) system. The Me group at the ester function is disordered in two positions, the calculated occupation factors are 0.69 and 0.31, respectively. Refinement proceeded to convergence at $R = 0.049$ with anisotropic refinement of all non-H-atoms. Coordinates and thermal parameters have been deposited with the *Crystallographic Data Centre*, Cambridge, University Chemical Lab., Cambridge CB2 1EW, UK.

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