Internal Nucleophilic Termination in Acid-Mediated Polyene Cyclizations

Part 5[1])

Synthetic Access to Didehydro Analogues of (±)-*Ambrox*® and Diastereoisomers

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Dedicated to Professor *Georg Fráter* on the occasion of his 65th birthday

Treatment of the acyclic tetraenols (*E*)- and (*Z*)-**2** with an excess of $ClSO_3H$ in 2-nitropropane at −80° stereoselectively afforded in 30 and 43% yield, respectively, diastereoisomer mixtures of the racemic, tricyclic ethers **1c**,**d** and **1a**,**b**, together with **20** (*Table*). Under identical conditions, but with the acyclic pentaenol **10** (1:1 diastereoisomer mixture) as substrate, the tricyclic ethers **22a**/**22b** (10:1) were isolated in 27% yield. These kinetically controlled stereospecific transformations are thought to proceed *via* non-concerted pathways (see *Schemes 5* and *7*), fully consistent with our earlier work. In contrast, another set of reaction conditions (CF_3CO_2H, CH_2Cl_2, −15° to −10°) was used for the cyclization of the monocyclic dienols (*E*)-**3** and (*Z*)-**3**, which resulted in the non-stereoselective formation of the major products **1c**,**d** and **1a**,**b**, respectively, in 35–37% yield. Representing novel didehydro analogues of the known ambergris odorant (±)-*Ambrox*® and its diastereoisomers, the qualitative organoleptic properties of **1a**–**d** and of the 10:1 diastereoisomer mixture of the novel tetradehydro analogues **22a**/**22b** are briefly described.

1. Introduction. – As part of a project designed to discover organoleptically active analogues of the labdane tricyclic ether *Ambrox*®, a commercially important, naturally occurring odorant [2], *Escher* and co-workers [3] synthesized in the 1980s the novel didehydro analogue (−)-**1d**, starting from either (+)-larixyl acetate or (+)-sclareolide, which itself is a precursor of *Ambrox*® and derived from the oxidative degradation of (−)-sclareol (*Scheme 1*)[2]). Because (−)-**1d**, aptly named *Superambrox* by *Firmenich* perfumers, exhibits an extremely powerful ambergris tonality, it was decided to develop a synthesis of the unknown racemate (±)-**1d**[3]), a potential odorant whose accessibility would not be dependent on a natural source. As a matter of fact, this strategy has been successfully used before for (±)-*Ambrox*, commercialized by *Firmenich SA* under the trade name *Cetalox*® [2].

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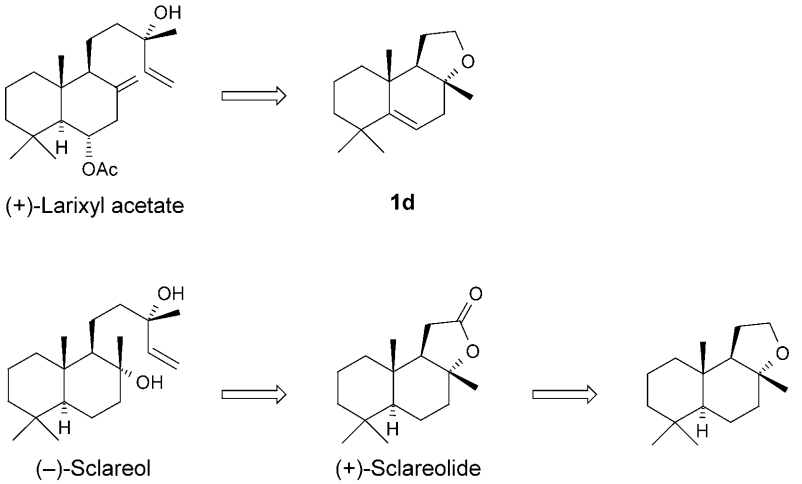
[1]) For Parts 1–4, see [1b–e].

[2]) For later, independent work by *de Groot* and co-workers, who also described the preparation of (−)-**1d** from (+)-larixyl acetate, see [4].

[3]) For a stereoselective synthesis of (±)-**1d**, see [5].

Scheme 1



A retrosynthetic analysis for the preparation of **1d** is shown in *Scheme 2*. Starting from the homoallylic alcohols (*E*)-**2** and (*E*)-**3** as direct precursors, **1d** should be accessible *via* acid-mediated cyclization. Thus, site-selective protonation of (*E*)-**2** or solvolysis of the allylic C–O bond of (*E*)-**3**[4]) would afford a diastereoisomer mixture of the cyclohexane-based allylic cations (*E*,*Z*)-**I** and (*E*,*E*)-**I**, of which only the latter, (*E*)-configured cation was expected to undergo further cyclization to **1d**. Although interconversion of (*E*,*Z*)-**I** and (*E*,*E*)-**I** under the reaction conditions cannot be completely discounted, this would necessarily involve quenching by an external nucleophile, followed by regeneration of the allylic cation (for a precedent of such an allyl-cation interconversion, involving a putative internal quenching, see [1d]).

Based on analogous previous work [1], we were confident that both (*E*)-**2** and (*E*)-**3** would form the desired *trans*-fused tetrahydrofuran ring *via trans* addition across the C(3)=C(4) bond. However, we were less sure about the stereoselectivity with respect to the C(9a)–Me group. Nevertheless, from inspection of models, it did not seem unreasonable to suppose that pseudoequatorial C–C bond formation opposite to the axially orientated C(6)–Me group would be kinetically favored. Notably, in related systems, a kinetic preference for equatorial C–C bond formation is generally observed for the cyclization of a cyclohexyl cation with an adjacent equatorial side chain [1].

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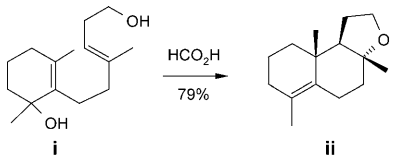
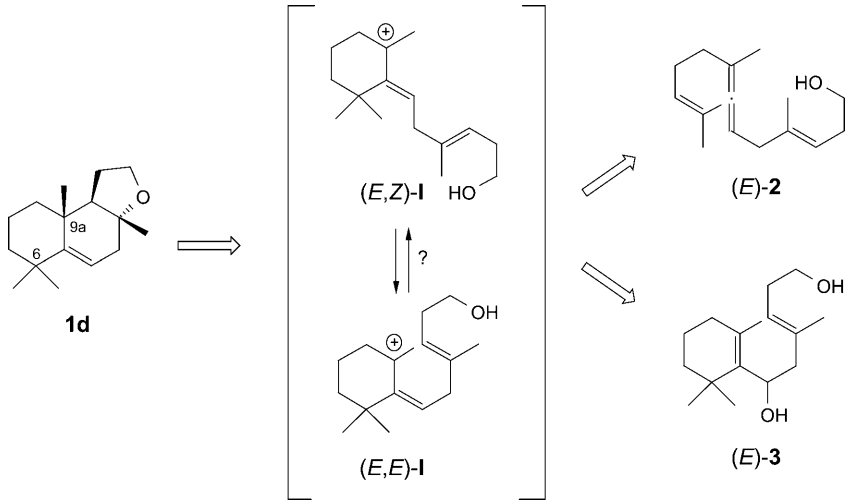
[4]) The putative conversion of (*E*)-**2** to **1** represents another example of an acid-mediated polyene cyclization in which the initiating group is an alkene and where termination is effected internally by an OH group [1]. In contrast, the transformation of (*E*)-**3** to **1** is analogous to the stereoselective cyclization of **i** to **ii** [6].



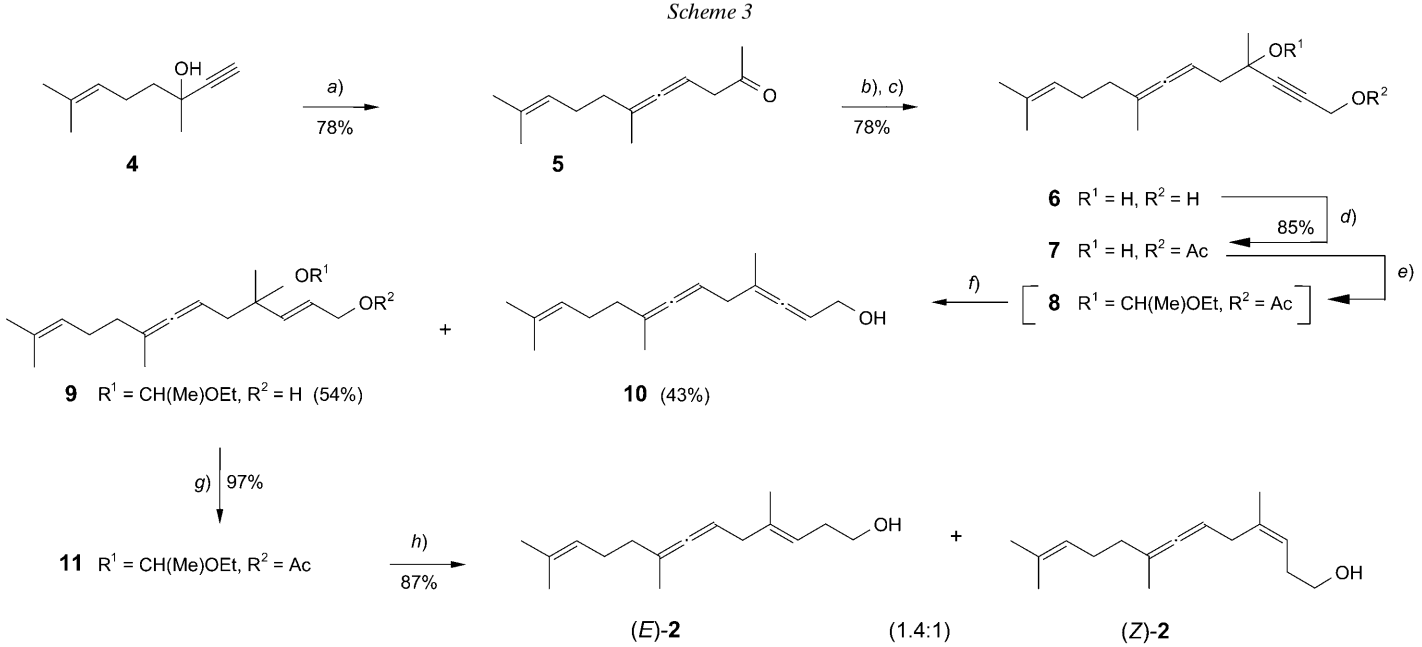
Scheme 2. *Retrosynthetic Analysis*



2. Results and Discussion. – 2.1. *Preparation of the Homoallylic Alcohols (*E*)-***2** *and (*Z*)-***2**. The synthetic approach towards **2** is outlined in *Scheme 3*. Following a reported procedure [7], dehydrolinalool (=3,7-dimethyloct-6-en-1-yn-3-ol; **4**) was converted to the trienone **5** *via Claisen* rearrangement in 78% yield. Low-temperature metalation of 3-[(trimethylsilyl)oxy]prop-1-yne with BuLi, followed by addition of **5** to the subsequent alkynyllithio species, afforded, after hydrolytic deprotection of the Me_3Si group, the trienynediol **6** in 78% overall yield. Next, the primary OH group was esterified to afford the acetate **7** in 85% yield, whose tertiary OH group was further protected as an acetal to afford **8**. The latter was immediately reduced with $LiAlH_4$ in THF at 20° to smoothly afford a 1.3:1 mixture of (*E*)-**9** and **10**, which, after chromatographic separation, were obtained in 54 and 43% yield, respectively. Reprotection of the primary OH group of **9** furnished the acetate **11** in 97% yield, which, on treatment with $LiAlH_4$ in THF/toluene at reflux, afforded in 87% yield a 1.4:1 mixture of (*E*)- and (*Z*)-**2** after chromatographic separation.

2.2. *Synthesis of the Homoallylic Alcohols* (*E*)-**3** *and (*Z*)-***3**. As shown in *Scheme 4*, treatment of β-cyclocitral (=2,6,6-trimethylcyclohex-1-ene-1-carbaldehyde; **12**) with 'methallyl chloride' (=3-chloro-2-methylprop-1-ene) and Mg in Et_2O at reflux under *Barbier* conditions gave the alcohol **13** (84% yield), which was protected as the *t*-Bu(Me)$_2$Si (TBDMS) ether **14** under standard conditions in 83% yield. Hydroboration of the latter with 9-borabicyclo[3.3.1]nonane (9-BBN) in THF, followed by oxidative hydrolysis, afforded the primary alcohol **15** as a 1.4:1 diastereoisomer mixture in 78% yield. Subsequent *Swern* oxidation cleanly gave the aldehyde **16** (1.4:1 diastereoisomer mixture), which then underwent a *Wadsworth–Emmons* reaction to furnish the α,β-unsaturated ester **17** as a 81:19 (*E*/*Z*) mixture (four diastereoisomers). Base-assisted isomerization of **17** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) at 95–98° resulted in the formation of an equilibrium mixture of **17** ((*E*/*Z*) 3:1; 24%) and the β,γ-unsaturated ester **18** ((*E*/*Z*) 1.9:1; 72%). This mixture was treated with $LiAlH_4$ in THF at reflux to afford, after chromatography, the alcohol **19** as an (*E*/*Z*)

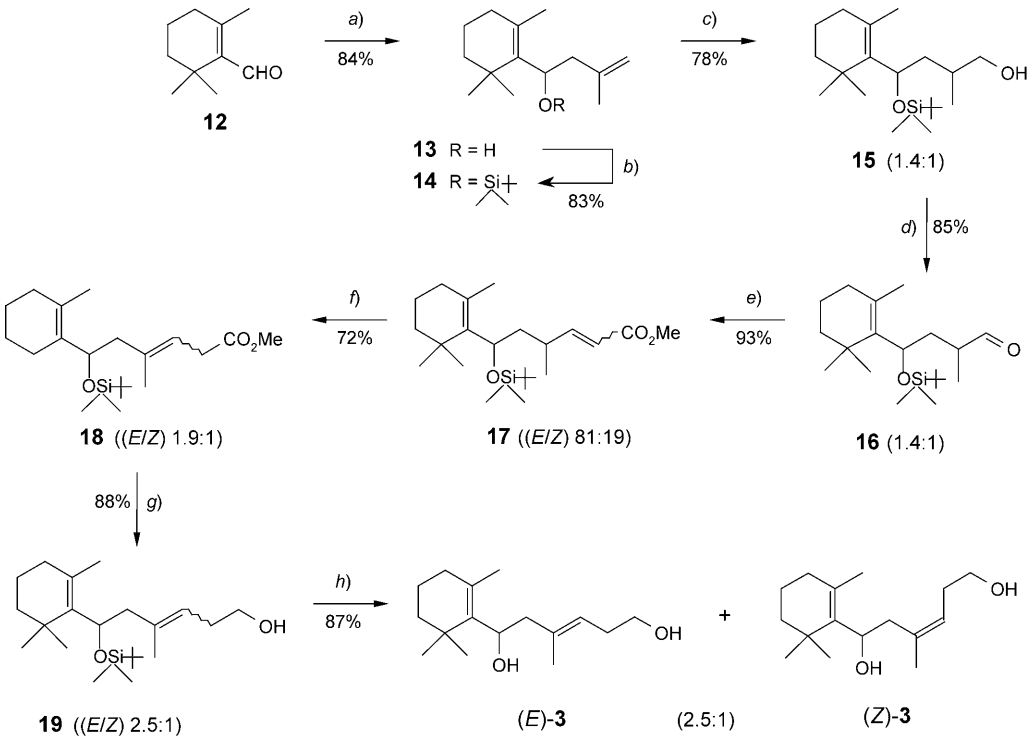
Scheme 3



a) 2-Methoxypropene, hydroquinone (cat.), $TsOH \cdot H_2O$ (cat.), petroleum ether, 80°. *b*) 3-[(Trimethylsilyl)oxy]prop-1-yne, BuLi, THF, −90°. *c*) 5% aq. HCl, r.t. *d*) Ac_2O, Et_3N, 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2, 2°. *e*) Ethyl vinyl ether, $TsOH \cdot H_2O$ (cat.), toluene, −10° to 0°. *f*) $LiAlH_4$, THF, 20°. *g*) Ac_2O, Et_3N, DMAP (cat.), toluene, r.t. *h*) $LiAlH_4$, THF, toluene, reflux. Note: Compounds **6**, **7**, and **10** were obtained as 1:1 diastereoisomer mixtures; compounds **8** and **9** were obtained as 1:1:1:1 diastereoisomer mixtures.

2.5 : 1 mixture in 88% yield. Hydrolysis of the TBDMS group with tetrabutylammonium fluoride trihydrate (TBAF) finally afforded the desired diol **3** as an (*E*/*Z*) 2.5 : 1 mixture in 87% yield. The diasteroisomers of **3** were readily separable by chromatography.

Scheme 4



a) 3-Chloro-2-methylprop-1-ene, Mg, Et_2O, reflux. *b*) NaH, ^{t}Bu(Me)$_2$SiCl, THF, reflux. *c*) 1. 9-Borabicyclo[3.3.1]nonane (9-BBN), THF, r.t.; 2. 3N aq. NaOH soln., 35% aq. H_2O_2 soln., 45°. *d*) Oxalyl chloride, DMSO, Et_3N, CH_2Cl_2, −55° to r.t. *e*) $(MeO)_2P(O)CH_2CO_2Me$, MeONa/MeOH, toluene, r.t. *f*) 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU), 95–98°. *g*) $LiAlH_4$, THF, reflux. *h*) $Bu_4NF \cdot 3\ H_2O$, THF, reflux.

2.3. *Acid-Mediated Cyclization of (*E*)-***2*** and (*Z*)-***2*** to the Tricyclic Ethers* **1a**–**1d**. The acid-mediated cyclizations of (*E*)- and (*Z*)-**2** were effected by treatment of each substrate with an excess of chlorosulfonic acid ($ClSO_3H$; 6 mol-equiv.) in 2-nitropropane at −80° during 15 min. Subsequent neutralization with aqueous Na_2CO_3 solution, extractive workup, and distillation *in vacuo* afforded the product mixtures in 30% and 43% yield, respectively. Pure samples of **1c**, **1d**, and **20** were obtained by column chromatography, and fully characterized spectroscopically. The 9 : 1 mixture of **1a**/**1b** was inseparable by chromatography. Nevertheless, structure assignment of each isomer was possible by in-depth NMR experiments.

The observed results are rationalized by kinetically controlled cyclizations, in analogy to our previous work [1]. A likely mechanistic rationale is presented in *Scheme 5*.

Thus, in a first step, protonation of the terminal trisubstituted C=C bond of (*E*)-**2** and (*Z*)-**2**, followed by cyclization, generates the cyclohexyl cations (*E*,*Z*)-**I** and (*E*,*E*)-**I** in the former case, and (*Z*,*Z*)-**I** and (*Z*,*E*)-**I** in the latter. Further cyclization of (*E*,*E*)-**I** and (*Z*,*E*)-**I**, considered to be concerted *via* simultaneous C–C and C–O bond formation, then occurs with good stereoselectivity to afford the tricyclic ethers **1c**/**1d** (3.8 : 1) and **1a**/**1b** (9 : 1), respectively. It is interesting to note that, in both cases, the MM2 energies of **1c** and **1d** (39.2 and 39.4 kcal/mol), and of **1a** and **1b** (35.3 and 36.8 kcal/mol) qualitatively reflect the observed selectivities. The cation (*Z*,*E*)-**I** also undergoes a concomitant cyclization/[1,2]-H shift to the cyclohexenyl cation **II**, energetically favored by the adjacent pseudoaxial H-atom, which then cyclizes to the tricyclic ether **20**. The structure of **20** was confirmed by NMR spectroscopy, where a marked NOE was observed between H–C(9) and Me–C(1). The low isolated yields of the products of these two cyclizations suggests that there is no rapid interconversion between (*E*,*Z*)-**I** and (*E*,*E*)-**I**, and between (*Z*,*Z*)-**I** and (*Z*,*E*)-**I**, respectively. It would thus appear likely that (*E*,*Z*)-**I** and (*Z*,*Z*)-**I** both lead to polymeric products under the highly acidic reaction conditions.

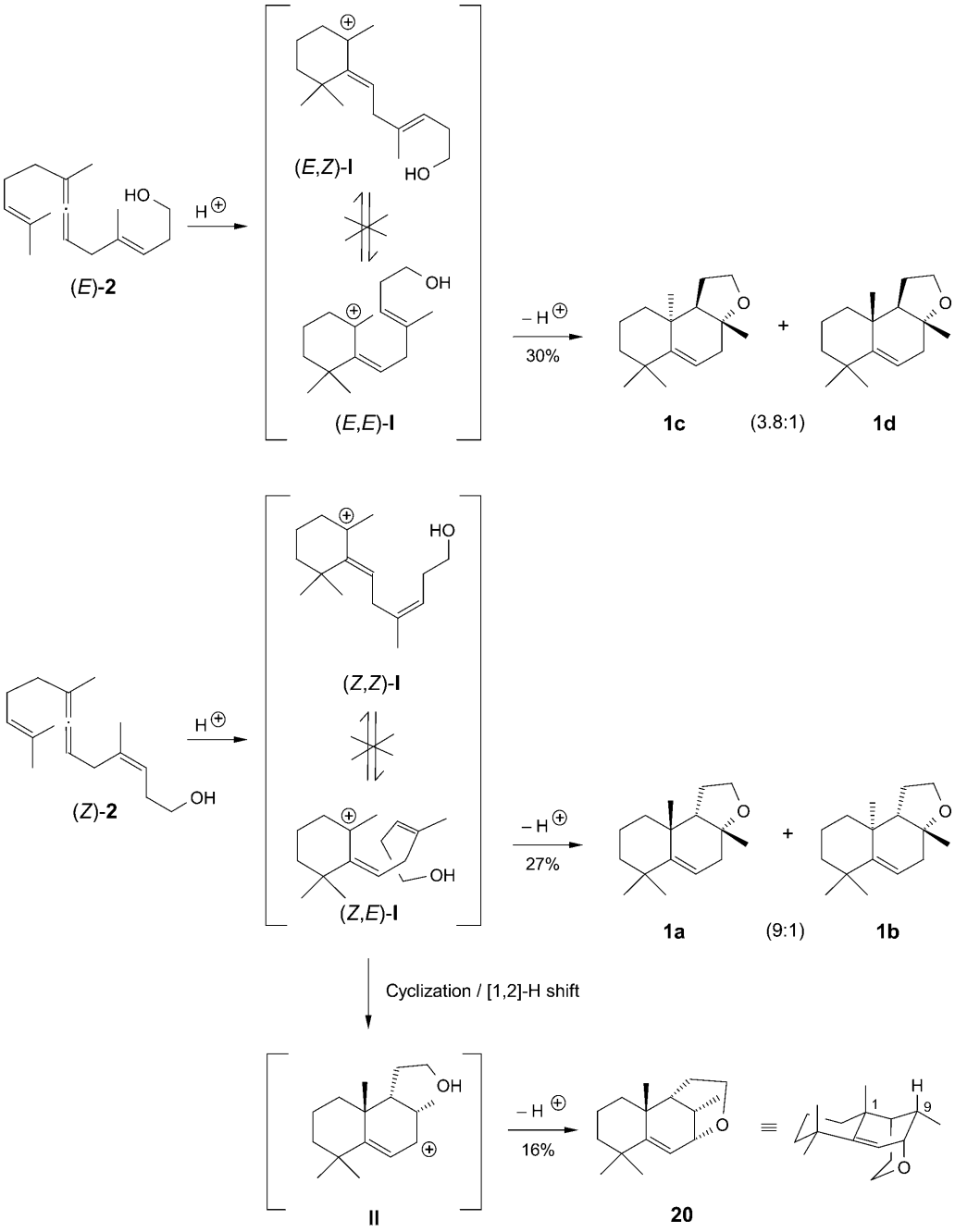
2.4. *Acid-Mediated Cyclization of (*E*)-***3*** and (*Z*)-***3*** to the Tricyclic Ethers* **1a**–**d**. In contrast, the acid-mediated cyclizations of (*E*)- and (*Z*)-**3** using $ClSO_3H$ in 2-nitropropane at $-80°$ afforded complex product mixtures containing only small amounts (*ca.* 5%) of the tricyclic ethers **1a**–**1d**, and were best conducted with a large excess of trifluoroacetic acid (TFA; 32 mol-equiv.) in CH_2Cl_2 at $-10°$ (*Scheme 6*). Subsequent neutralization with aqueous Na_2CO_3 solution, extractive workup, and distillation *in vacuo* afforded the product mixtures in 35% and 37% yield, respectively. The product distribution was determined by analytical gas chromatography (*Table*). The compounds **1a**–**1d** were identified by comparison with authentic samples, and the tetrahydrofuran **21** was isolated by column chromatography, and characterized by mass spectrometry and NMR spectroscopy[5]).

The observed results are consistent with a mechanism first involving heterolysis of the allylic C–O bond in (*E*)- and (*Z*)-**3** to afford the same allylic cations, (*E*,*Z*)-**I**/(*E*,*E*)-**I** and (*Z*,*Z*)-**I**/(*Z*,*E*)-**I**, respectively, as proposed for the cyclizations of (*E*)-**2** and (*Z*)-**2** (*vide supra*). Not surprisingly, in view of the harsher reaction conditions, subsequent cyclization proceeds with lower stereoselectivity with respect to C–C bond formation. In the former case, **1c**/**1d** (1.3 : 1; 27% yield) and **1b** (< 1% yield) were formed, whereas in the latter case **1a**/**1b** (1.4 : 1; 32% yield) and **1d** (< 0.5% yield) were obtained. In both cases, small amounts (7 and 5%, resp.) of **21** were isolated, a product resulting from C–O bond formation *via* protonation at C(3) (see *Scheme 6*).

2.5. *Acid-Mediated Cyclization of* **10** *to the Tricyclic Ethers* **22a**,**b**. Acid-mediated cyclization of **10** (1 : 1 diastereoisomer mixture), under conditions identical to those employed for (*E*)- and (*Z*)-**2** (excess of $ClSO_3H$ at $-80°$), furnished **22a**/**22b** 10 : 1 in 27% yield (*Scheme 7*). Once again, this result may be rationalized by a kinetically controlled, stepwise process. In a first step, **10** cyclizes non-stereoselectively to the cyclohexyl cations (*E*/*Z*)-**III**, whereupon the former cation then undergoes a second cyclization to afford the allylic cation **IV** as a '*syn*'/'*anti*' diastereoisomer mixture. Only '*syn*'-

[5]) Structure determinations were greatly facilitated by comparison with the NMR spectra of analogous tricyclic ethers from earlier work [1].

Scheme 5. *Acid-Mediated Cyclizations of (*E*)- and (Z)-***2***, and Mechanistic Rationale for the Formation of* **1a**–**d** *and* **20**



Scheme 6. *Acid-Mediated Cyclizations of* (E)- *and* (Z)-**3**, *and Mechanistic Rationale for the Formation of* **1a–d** *and* **21**

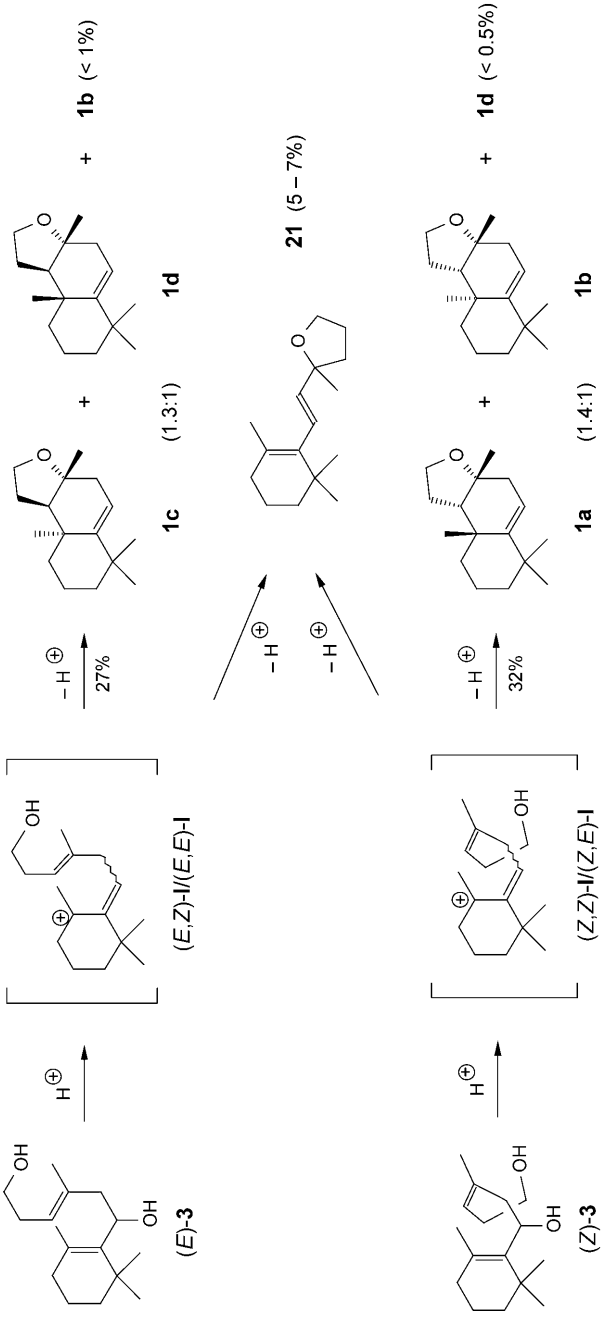


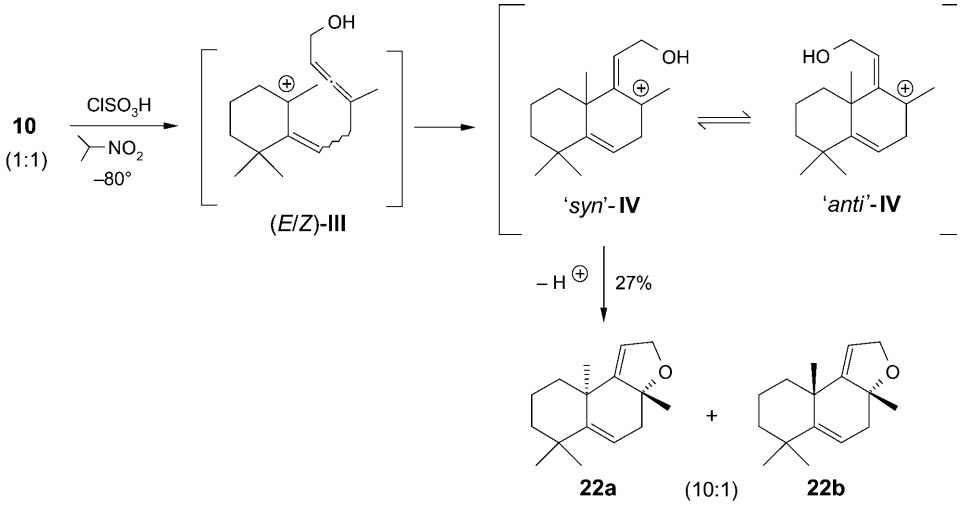
Table. *Results of Acid-Mediated Cyclizations of Compounds* **2** *and* **3**. For details, see Exper. Part.

Substrate	Condition[a])	Product distribution [%][b])						Yield [%]
		1a	**1b**	**1c**	**1d**	**20**	**21**	
(*E*)-**2**	*A*	–	–	79	21	–	–	30
(*Z*)-**2**	*A*	57	6	–	–	37	–	43
(*E*)-**3**	*B*		2	45	34	–	19	35
(*Z*)-**3**	*B*	50	36	–	1	–	13	37

[a]) *A*: Substrate (0.3 g), $ClSO_3H$ (0.5 ml), 2-nitropropane (15 ml), $-80°$; *B*: substrate (0.4 g), CF_3CO_2H (4 ml), CH_2Cl_2 (40 ml), $-15°$ to $-10°$. [b]) According to GC analysis of the distilled product after workup.

IV can undergo subsequent C–O bond formation and ring closure to **22**, but a precedent in a closely analogous system [1d] indicated that '*anti*'-**IV** also leads to the same product mixture *via* rapid interconversion of the '*syn*' and '*anti*' diastereoisomers. In analogy with the cyclizations of (*E*)-**2** and (*Z*)-**2** (*vide supra*), it is noteworthy that the MM2 energies of **22a** and **22b** (33.7 and 36.1 kcal/mol, resp.) qualitatively mirror the observed selectivity for the former diastereoisomer.

Scheme 7. *Acid-Mediated Cyclization of* **10** (1:1 diastereoisomer mixture) *and Mechanistic Rationale for the Formation of* **22a**,**b**



2.6. *Organoleptic Properties of* **1a**–**1d**, **20**, *and* **22a**,**b**. Due to the small amounts of compounds available, qualitative rather than quantitative odor evaluations were effected. Thus, in comparison with racemic *Ambrox*, the didehydro analogues **1a**–**1d** were all perceived as *amber and woody*, though **1d** clearly stood out as being the most powerful of the four diastereoisomers. In contrast, the tetrahydropyran **20** only exhibited *weak woody* notes. Finally, the tetradehydro analogues **22a**/**22b** (10:1) also possessed *strong ambery-woody* tonalities.

3. Conclusions. – Synthetic access to racemic didehydro and tetradehydro analogues of the labdane tricyclic ether *Ambrox* was achieved, and their organoleptic properties have been qualitatively evaluated. The described results provide further examples of *Brønsted* acid-mediated polyene cyclizations, in which the initiating group is an alkene and the terminating group is an alcohol. Although these cyclizations do not always occur with high stereoselectivity, and proceed in only fair yields, the methodology is suited to access tricyclic ethers from readily available starting materials, ethers that would be difficult to prepare by other methods.

We thank Mr. *W. Thommen* and Mr. *R. Brauchli* for the measurement and interpretation of NMR spectra. Dr. *B. Winter* and Dr. *J.-Y. de Saint Laumer* are kindly acknowledged for performing MM2 calculations.

Experimental Part

General. See [1d]. GC Retention times (t_R, in min) refer to the following conditions: *SPB1* column (15 m; i.d. 0.25 mm), 150–220° at 10°/min, He flow at 10 ml/min.

6,10-Dimethylundeca-4,5,9-trien-2-one (**5**). A mixture of 3,7-dimethyloct-6-en-1-yn-3-ol (**4**; 20 g, 0.13 mol), 2-methoxypropene (28 g, 0.39 mol), hydroquinone (60 mg), and $TsOH \cdot H_2O$ (20 mg) in petroleum ether (b.p. 80–100°, 50 ml) was heated at reflux under N_2 during 16 h. After cooling to 25°, a soln. of AcONa (20 mg) in MeOH (2 ml) was added, and the mixture was evaporated and fractionally distilled *in vacuo* to afford **5** (19.5 g, 78%). Pale-yellow oil. B.p. 57–59°/0.05 mbar. R_f 0.65 (cyclohexane/AcOEt 7:3). IR: 2916, 1719, 1443, 1356, 1222, 1156. ^{1}H-NMR: 1.60 (*s*, 3 H); 1.69 (*s*, 3 H); 1.69 (*d*, J=3, 3 H); 1.97 (2 H); 2.09 (2 H); 2.18 (*s*, 3 H); 3.05 (*d*, J=7, 2 H); 5.05–5.17 (*m*, 1 H); 5.10–5.20 (*m*, 1 H). ^{13}C-NMR: 17.7 (*q*); 18.9 (*q*); 25.7 (*q*); 26.3 (*t*); 29.1 (*q*); 34.1 (*t*); 44.7 (*t*); 83.5 (*d*); 100.4 (*s*); 124.2 (*d*); 131.7 (*s*); 203.2 (*s*); 206.7 (*s*). MS: 192 (1, M^+), 134 (9), 119 (11), 109 (100), 81 (34), 69 (48).

3-[(Trimethylsilyl)oxy]prop-1-yne. Me_3SiCl (21.7 g, 0.2 mol) was added dropwise during 15 min to a stirred soln. of prop-2-yn-1-ol (11.2 g, 0.2 mol) and 1*H*-imidazole (15 g, 0.22 mol) in DMF (100 ml) at 10° under N_2. The mixture was allowed to attain 20° during 14 h, and then poured into sat. aq. $NaHCO_3$ soln. Extraction with pentane, workup, evaporation at 760 mbar, and fractional distillation afforded the title compound (18.5 g, 72%). B.p. 85–88°/760 mbar. ^{1}H-NMR: 0.12 (*s*, 9 H); 2.34 (*t*, J=2.5, 1 H); 4.22 (*d*, J=2.5, 2 H). MS: 128 (<0.5, M^+), 113 (85), 83 (100).

4,8,12-Trimethyltrideca-6,7,11-trien-2-yne-1,4-diol (**6**). A 1.6M hexane soln. of BuLi (38 ml) was added dropwise during 30 min to a stirred soln. of *3-[(trimethylsilyl)oxy]prop-1-yne* (13 g, 70 mmol) in THF (75 ml) at −90° under N_2. After a further 30 min at −90°, a soln. of **5** (10 g, 052 mmol) in THF (25 ml) was added dropwise during 25 min, and, after a further 2 h, the mixture was poured into sat. aq. NH_4Cl soln. (300 ml). Extraction with Et_2O was followed by vigorous stirring of the org. phase with 5% aq. HCl (80 ml) at 20° during 2 h. Separation of the org. phase was followed by washing to neutrality with sat. aq. $NaHCO_3$ soln. and brine. Workup, CC (cyclohexane/AcOEt 4:1), and evaporation at 5°/0.05 mbar afforded **6** as a 1:1 diastereoisomer mixture (9.2 g, 78%). R_f 0.14 (cyclohexane/AcOEt 7:3). ^{1}H-NMR (after exchange with D_2O): 1.51 (*s*, 3 H); 1.61 (*s*, 3 H); 1.69 (*s*, 3 H); 1.70 (*d*, J=3, 3 H); 1.97 (2 H); 2.11 (2 H); 2.30 (*ddd*, J=14, 8, 2.5, 1 H); 2.38 (*dd*, J=14, 8, 1 H); 4.29 (*s*, 2 H); 5.13 (2 H). ^{13}C-NMR: 17.7 (*q*); 19.1, 19.3 (2*q*); 25.7 (*q*); 26.3 (*t*); 29.0 (*q*); 34.1, 34.2 (2*t*); 44.3 (*t*); 50.9 (*t*); 67.6 (*s*); 81.8 (*s*); 85.0 (*d*); 89.3 (*s*); 99.3, 99.4 (2*s*); 124.1, 124.2 (2*d*); 131.8, 131.9 (2*s*); 203.9 (*s*). MS: 248 (<0.5, M^+), 230 (3), 212 (12), 197 (16), 169 (20), 129 (35), 91 (47), 69 (59), 41 (100).

4-Hydroxy-4,8,12-trimethyldeca-6,7,11-trien-2-yn-1-yl Acetate (**7**). Et_3N (6.6 ml, 47 mmol) was added dropwise during 15 min to a stirred soln. of **6** (9 g, 36 mmol) and Ac_2O (4.2 ml, 44 mmol) in CH_2Cl_2 (10 ml) at 0–2°. After a further 90 min (conversion almost complete by TLC analysis), 4-(dimethylamino)-pyridine (DMAP; 15 mg) was added and, 30 min later, the mixture was poured into cold 10% aq. HCl. Extraction with Et_2O, workup, CC (cyclohexane/AcOEt 4:1), and evaporation at 50°/0.05 mbar afforded **7** as a 1:1 diastereoisomer mixture (9.9 g, 85%). Attempted distillation *in vacuo* resulted in extensive

decomposition. R_f 0.40 (cyclohexane/AcOEt 7:3). ^{1}H-NMR (after exchange with D_2O): 1.51 (*s*, 3 H); 1.60 (*s*, 3 H); 1.69 (*s*, 3 H); 1.70 (*d*, *J* = 3, 3 H); 1.98 (2 H); 2.10 (*s*, 3 H); 2.11 (2 H); 2.29 (br. *d*, *J* = 14, 8, 1 H); 2.38 (*dd*, *J* = 14, 8, 1 H); 4.70 (*s*, 2 H); 5.06–5.18 (2 H). MS (more-volatile diastereoisomer): 290 (< 0.5, M^+), 212 (28), 197 (30), 187 (21), 169 (36), 144 (35), 129 (38), 69 (46), 43 (100). MS (less-volatile diastereoisomer): 290 (< 0.5, M^+), 212 (27), 197 (25), 187 (12), 169 (37), 144 (38), 128 (37), 69 (48), 43 (100).

(2E)-4-[(1-Ethoxyethyl)oxy]-4,8,12-trimethyltrideca-2,6,7,11-tetraen-1-ol (**9**) *and 4,8,12-Trimethyltrideca-2,3,5,6,11-pentaen-1-ol* (**10**). A soln. of ethyl vinyl ether (3 g, 42 mmol) in toluene (5 ml) was added dropwise during 10 min to a stirred soln. of **7** (5.6 g, 19 mmol) and $TsOH \cdot H_2O$ (40 mg) in toluene (25 ml) at −10° under N_2. After 2 h at 0°, the mixture was poured into sat. aq. $NaHCO_3$ soln. and extracted with Et_2O. Workup, CC (cyclohexane/AcOEt 9:1), and evaporation at 60°/0.05 mbar afforded crude *4-[(1-ethoxyethyl)oxy]-4,8,12-trimethyltrideca-6,7,11-trien-2-yn-1-yl acetate* (**8**) as a diastereoisomer mixture (6.1 g, 87%; R_f 0.48 (cyclohexane/AcOEt 4:1)), which was used without further purification. Thus, a soln. of **8** (5.5 g, 15 mmol) in THF (25 ml) was added dropwise during 30 min to a stirred suspension of $LiAlH_4$ (0.68 g, 18 mmol) in THF (15 ml) at 20° under N_2. After a further 30 min, the mixture was cooled to 10°, and H_2O (0.68 ml), 15% aq. NaOH soln. (0.68 ml), and H_2O (2 ml) were successively added dropwise under vigorous stirring. After 30 min at 20°, the mixture was filtered (*Hyflo*) and the filtrate was evaporated *in vacuo* to afford a residual oil (4.9 g). CC (cyclohexane/AcOEt 4:1) and evaporation at 40°/0.05 mbar furnished the more polar product **9** as a 1:1:1:1 diastereoisomer mixture (2.6 g, 54%), and the less polar product **10** as a 1:1 diastereoisomer mixture (1.5 g, 43%). Attempted distillation *in vacuo* resulted in extensive decomposition.

Data of **9**. R_f 0.15 (cyclohexane/AcOEt 4:1). ^{1}H-NMR (after exchange with D_2O): 1.16 (*t*, *J* = 7, 3 H); 1.27, 1.28 (2*d*, *J* = 7, 3 H); 1.31, 1.37 (2*s*, 3 H); 1.60 (*s*, 3 H); 1.66, 1.67 (2*d*, *J* = 2, 3 H); 1.69 (*s*, 3 H); 1.93 (2 H); 2.08 (br. *dt*, *J* = 7, 7, 2 H); 2.24 (2 H); 3.42–3.59 (*m*, 2 H); 4.13–4.19 (2 H); 4.81 (*q*, *J* = 6, 1 H); 4.94–5.02 (*m*, 1 H); 5.12 (br. *t*, *J* = 7, 1 H); 5.70–5.85 (*m*, 2 H). ^{13}C-NMR: 15.4, 15.5 (2*q*); 17.7 (*q*); 19.1 (*q*); 21.5, 21.9 (2*q*); 23.1, 23.2 (2*q*); 25.7, 26.3 (2*q*); 34.1 (*t*); 41.9, 42.1, 42.2 (3*t*); 58.3, 59.1 (2*t*); 63.3 (*t*); 85.6, 85.7 (2*d*); 94.4, 94.6 (2*d*); 98.4 (*s*); 124.3 (*d*); 129.2, 129.5 (2*d*); 131.6 (*s*); 136.2, 136.5 (2*d*); 203.1 (*s*). MS: 322 (< 0.5, M^+), 145 (14), 73 (100),

Data of **10**. R_f 0.45 (cyclohexane/AcOEt 4:1). ^{1}H-NMR (after exchange with D_2O): 1.60 (*s*, 3 H); 1.68 (6 H); 1.75, 1.76 (2*s*, 3 H); 1.95 (2 H); 2.09 (br. *dt*, *J* = 7, 7, 2 H); 2.65 (*d*, *J* = 7, 2 H); 4.07 (*d*, *J* = 6, 2 H); 5.00 (*m*, 1 H); 5.13 (br. *t*, *J* = 7, 1 H); 5.27 (*m*, 1 H). ^{13}C-NMR: 17.7 (*q*); 18.6 (*q*); 19.2, 19.3 (2*q*); 25.7 (*q*); 26.3 (*t*); 34.2 (*t*); 35.0 (*t*); 60.8, 60.9 (2*t*); 87.8 (*d*); 91.3 (*d*); 99.7 (*s*); 102.2 (*s*); 124.2 (*d*); 131.6 (*s*); 200.4 (*s*); 201.9 (*s*). MS: 232 (1, M^+), 189 (46), 145 (69), 105 (36), 91 (41), 69 (62), 43 (100).

(2E)-4-[(1-Ethoxyethyl)oxy]-4,8,12-trimethyltrideca-2,6,7,11-tetraen-1-yl Acetate (**11**). Et_3N (1.35 ml, 9.6 mmol) was added dropwise during 10 min to a stirred mixture of **9** (2.5 g, 7.7 mmol), Ac_2O (0.9 ml, 9.4 mmol), and DMAP (10 mg) in toluene (12 ml) at r.t. under N_2. After a further 2 h at 35–40°, the cooled mixture was poured into cold 5% aq. HCl soln. (15 ml) and extracted with Et_2O. Workup, filtration through silica gel (cyclohexane/AcOEt 9:1), and evaporation at 50°/0.04 mbar afforded **11** as a 1:1:1:1 diastereoisomer mixture (2.75 g, 97%). R_f 0.26 (cyclohexane/AcOEt 9:1). ^{1}H-NMR: 1.17 (2*t*, *J* = 7, 3 H); 1.27, 1.29 (2*d*, *J* = 7, 3 H); 1.31, 1.37 (2*s*, 3 H); 1.60 (*s*, 3 H); 1.66, 1.67 (2*d*, *J* = 2, 3 H); 1.69 (*s*, 3 H); 1.90–1.96 (*m*, 2 H); 2.07 (*s*, 3 H); 2.03–2.13 (*m*, 2 H); 2.20–2.30 (*m*, 2 H); 3.37–3.57 (2 H); 4.58 (*d*, *J* = 6, 2 H); 4.73–4.81 (*m*, 1 H); 4.92–5.02 (*m*, 1 H); 5.11 (br. *t*, *J* = 7, 1 H); 5.65–5.92 (*m*, 2 H). ^{13}C-NMR: 15.4 (*q*); 17.7 (*q*); 19.1 (*q*); 20.9 (*q*); 21.5, 22.0 (2*q*); 23.0, 23.1 (2 *q*); 25.7 (*q*); 26.3 (*t*); 34.1 (*t*); 41.8, 42.1 (2*t*); 59.8 (*t*); 64.7 (*t*); 85.4 (*d*); 94.7 (*d*); 98.4 (*s*); 123.8, 124.3 (2*d*); 131.5 (*s*); 139.4, 139.6 (2*d*); 170.7 (*s*); 203.1 (*s*). MS: 364 (< 0.5, M^+), 145 (9), 91 (11), 73 (100).

4,8,12-Trimethyltrideca-3,6,7,11-tetraen-1-ol (**2**). A soln. of **11** (2.6 g, 7.1 mmol) in THF (12 ml) was added dropwise during 20 min to a stirred slurry of $LiAlH_4$ (0.33 g, 8.7 mmol) in THF (8 ml) at 50° under N_2, and the mixture was then heated at reflux for 5 d. Toluene was added, and the mixture was heated at reflux for a further 24 h. The mixture was cooled at 10°, and successively treated dropwise with H_2O (0.33 ml), 15% aq. NaOH soln. (0.33 ml), THF (20 ml), and H_2O (1 ml). Filtration (*Hyflo*), concentration of the filtrate *in vacuo*, CC (toluene, AcOEt 9:1), and evaporation at 50°/0.04 mbar afforded **2** as a 1.4:1 (*E*/*Z*)-mixture (1.45 g, 87%). Further purification by CC led to the isolation of (*E*)-**2** (0.51 g) and (*Z*)-**2** (0.44 g).

Data of (*E*)-**2**. R_f 0.58 (toluene/AcOEt 85:15). ^{1}H-NMR (after exchange with D_2O): 1.60 (*s*, 3 H); 1.68 (*s*, 3 H); 1.69 (*s*, 3 H); 1.75 (*s*, 3 H); 1.91–1.99 (*m*, 2 H); 2.09 (br. *dt*, *J*=7, 7, 2 H); 2.30 (*dt*, *J*=7, 7, 2 H); 2.71 (*d*, *J*=7, 2 H); 3.61 (br. *t*, *J*=6, 2 H); 4.93–5.01 (*m*, 1 H); 5.10–5.16 (*m*, 1 H); 5.18 (br. *t*, *J*=7, 1 H). ^{13}C-NMR: 16.2 (*q*); 17.7 (*q*); 19.2 (*q*); 25.7 (*q*); 26.4 (*t*); 31.6 (*t*); 34.2 (*t*); 40.2 (*t*); 62.2 (*t*); 88.8 (*d*); 99.3 (*s*); 120.6 (*d*); 124.3 (*d*); 131.5 (*s*); 138.0 (*s*); 202.0 (*s*). MS: 234 (<0.5, M^+), 219 (4), 191 (17), 173 (18), 147 (34), 135 (39), 119 (59), 105 (65), 91 (48), 69 (53), 41 (100).

Data of (*Z*)-**2**. R_f 0.63 (toluene/AcOEt 85:15). ^{1}H-NMR (after exchange with D_2O): 1.60 (*s*, 3 H); 1.68 (*s*, 3 H); 1.69 (2*s*, 6 H); 1.92–1.97 (*m*, 2 H); 2.08 (br. *dt*, *J*=7, 7, 2 H); 2.30 (*dt*, *J*=7, 7, 2 H); 2.67 (*d*, *J*=7, 2 H); 3.61 (br. *t*, *J*=6, 2 H); 4.94–5.02 (*m*, 1 H); 5.10–5.16 (*m*, 1 H); 5.20 (br. *t*, *J*=7, 1 H). ^{13}C-NMR: 17.7 (*q*); 19.2 (*q*); 23.6 (*q*); 25.7 (*q*); 26.4 (*t*); 31.4 (*t*); 32.4 (*t*); 34.3 (*t*); 62.4 (*t*); 88.2 (*d*); 99.7 (*s*); 121.0 (*d*); 124.3 (*d*); 131.6 (*s*); 137.8 (*s*); 201.8 (*s*). MS: 234 (<0.5, M^+), 219 (3), 191 (18), 173 (18), 147 (32), 135 (37), 119 (55), 105 (61), 93 (50), 69 (53), 41 (100).

*Acid-Mediated Cyclization of (*E)-**2**. A soln. of (*E*)-**2** (0.3 g, 1.28 mmol) in 2 nitropropane (6 ml) was added dropwise during 20 min to a mechanically stirred soln. of $ClSO_3H$ (0.5 ml, 7.5 mmol) in 2-nitropropane (9 ml) at −80° under N_2. After 15 min at −80°, sat. aq. Na_2CO_3 soln. (6 ml) was added to the orange mixture, which was then allowed to attain 20° over 1 h. Extraction with Et_2O, workup, CC (cyclohexane/AcOEt 19:1), and bulb-to-bulb distillation *in vacuo* (140–150°/0.04 mbar) afforded a 79:21 mixture of **1c**/**1d** (90 mg, 30%) as a pale-yellow oil. Repeated CC (cyclohexane/AcOEt 19:1) afforded anal. pure samples (*ca*. 10–15 mg) of each diastereoisomer.

*Data of (3a*RS*,9a*SR*,9b*RS*)-1,2,3a,4,6,7,8,9,9a,9b-Decahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan* (**1c**). R_f 0.26 (cyclohexane/AcOEt 9:1). GC: t_R 3.72. IR ($CHCl_3$): 2966, 1465, 1363, 1290, 1143, 1087, 1044, 995. ^{1}H-NMR: 1.04 (*s*, 3 H); 1.09 (*s*, 3 H); 1.19 (*s*, 3 H); 1.26 (*s*, 3 H); 3.82–3.92 (*m*, 1 H); 3.94–4.01 (*m*, 1 H); 5.49 (*dd*, *J*=6, 3, 1 H). ^{13}C-NMR: 19.3 (*t*, C(8)); 19.4 (*q*, Me−C(3a)); 23.2 (*t*, C(1)); 28.2 (*q*, Me_α−C(6)); 29.8 (*q*, C(9a)); 32.5 (*t*, C(9)); 33.8 (*q*, Me_β−C(6)); 37.1 (*s*, C(6)); 39.6 (*s*, C(9a)); 40.5 (*t*, C(4)); 42.0 (*t*, C(7)); 56.4 (*d*, C(9b)); 65.6 (*t*, C(2)); 79.4 (*s*, C(3a)); 118.1 (*d*, C(5)); 150.4 (*s*, C(5a)). MS: 234 (2, M^+), 219 (3), 150 (63), 135 (99), 105 (26), 84 (100).

*Data of (3a*RS*,9a*RS*,9b*RS*)-1,2,3a,4,6,7,8,9,9a,9b-Decahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan* (**1d**). R_f 0.30 (cyclohexane/AcOEt 9:1). GC: t_R 3.86. IR ($CHCl_3$): 2929, 1472, 1378, 1142, 1046, 993. ^{1}H-NMR: 1.06 (*s*, 3 H); 1.09 (*s*, 3 H); 1.13 (*s*, 3 H); 1.14 (*s*, 3 H); 1.20–1.30 (*m*, 1 H); 2.20–2.28 (*m*, 2 H); 3.85 (*ddd*, *J*=8, 8, 8, 1 H); 3.98 (*ddd*, *J*=9, 8, 3, 1 H); 5.44 (*dd*, *J*=4, 4, 1 H). ^{13}C-NMR: 18.3 (*t*, C(8)); 19.5 (*q*, Me−C(9a)); 21.8 (*q*, Me−C(3a)); 23.5 (*t*, C(1)); 29.0 (*q*, Me_β−C(6)); 33.2 (*q*, Me_α−C(6)); 36.3 (*s*, C(6)); 38.4 (*s*, C(9a)); 41.5 (*t*, C(4)); 42.0 (*t*, C(7)); 42.3 (*t*, C(9)); 57.3 (*d*, C(9b)); 65.4 (*t*, C(2)); 78.3 (*s*, C(3a)); 117.6 (*d*, C(5)); 149.9 (*s*, C(5a)). MS: 234 (1, M^+), 219 (9), 150 (59), 135 (82), 105 (21), 84 (100).

*Acid-Mediated Cyclization of (*Z)-**2**. Using the same procedure as described above, (*Z*)-**2** (0.3 g, 1.28 mmol) was treated with $ClSO_3H$ (0.5, l, 7.5 mmol) to afford, after CC (cyclohexane/AcOEt 19:1) and bulb-to-bulb distillation (140–150°/0.04 mbar), a 57:6:37 mixture of **1a**/**1b**/**20** (130 mg, 43%). Repeated CC (cyclohexane/toluene/AcOEt 10:9:1) afforded an inseparable 9:1 mixture of **1a**/**1b** (*ca*. 20 mg) and **20** (20 mg).

*Data of (3a*RS*,9a*RS*,9b*SR*)-1,2,3a,4,6,7,8,9,9a,9b-Decahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan* (**1a**). R_f 0.33 (cyclohexane/AcOEt 9:1). GC: t_R 3.28. ^{1}H-NMR: 1.07 (*s*, 3 H); 1.11 (*s*, 3 H); 1.14 (*s*, 3 H); 1.36 (*s*, 3 H); 1.20–1.80 (8 H); 1.92–1.99 (*m*, 1 H); 2.09 (*dd*, *J*=18, 3, 1 H); 2.39 (*dd*, *J*=18, 6, 1 H); 3.49–3.55 (*m*, 1 H); 3.71 (*ddd*, *J*=6, 6, 2, 1 H); 5.58 (*dd*, *J*=6, 3, 1 H). ^{13}C-NMR: 17.7 (*t*, C(8)); 25.8 (*q*, Me−C(9a)); 30.1 (*q*, Me−C(3a)); 31.4 (*q*, Me_α−C(6)); 32.2 (*q*, Me_β−C(6)); 33.1 (*t*, C(1)); 34.8 (*s*, C(6)); 37.1 (*t*, C(4)); 37.2 (*t*, C(9)); 37.9 (*s*, C(9a)); 40.1 (*t*, C(7)); 57.9 (*d*, C(9b)); 64.1 (*t*, C(2)); 80.8 (*s*, C(3a)); 117.9 (*d*, C(5)); 148.7 (*s*, C(5a)). MS: 234 (14, M^+), 150 (33), 135 (100), 107 (14), 84 (61).

*Data of (3a*RS*,9a*SR*,9b*SR*)-1,2,3a,4,6,7,8,9,9a,9b-Decahydro-3a,6,6,9a-tetramethylnaphtho[2.1-b]furan* (**1b**). R_f 0.33 (cyclohexane/AcOEt 9:1). GC: t_R 3.53. ^{1}H-NMR: 1.01 (*s*, 3 H); 1.10 (*s*, 3 H); 1.11 (*s*, 3 H); 1.13 (*s*, 3 H); 0.80–1.80 (7 H); 1.81–1.90 (*m*, 1 H); 1.95–2.02 (*m*, 1 H); 2.25–2.35 (*m*, 2 H); 3.79–3.87 (*m*, 2 H); 5.63 (*dd*, *J*=7, 3.5, 1 H). ^{13}C-NMR: 18.2 (*t*, C(8)); 19.9 (*q*, Me−C(9a)); 26.7 (*t*, C(1)); 29.4 (*q*, Me_α−C(6)); 32.2 (*q*, Me−C(3a)); 32.4 (*q*, Me_β−C(6)); 35.2 (*s*, C(6)); 36.5 (*t*, C(4)); 37.8 (*t*, C(9a)); 39.9 (*s*, C(7) or C(9)); 40.0 (*t*, C(9) or C(7)); 57.3 (*d*, C(9b)); 65.9 (*t*, C(2)); 77.9 (*s*, C(3a)); 118.3 (*d*, C(5)); 152.7 (*s*, C(5a)). MS: 234 (6, M^+), 150 (56), 135 (100), 107 (12), 84 (76).

*Data of (2*SR*,6*RS*,6a*RS*,11*SR*)-4,5,6,6a,7,8,9,10-Octahydro-6a,10,10,11-tetramethyl-2,6-methano-2*H*-3-benzoxocin* (**20**). R_f 0.40 (cyclohexane/AcOEt 9:1). GC: t_R 3.87. ^{1}H-NMR: 1.13 (*s*, 3 H); 1.14 (*s*, 3 H); 1.24 (*d*, *J*=7, 3 H); 1.26 (*s*, 3 H); 1.20–1.70 (7 H); 1.82–1.96 (*m*, 2 H); 2.03–2.11 (*m*, 1 H); 3.43 (*dd*, *J*=11, 7, 1 H); 3.68–3.77 (*m*, 1 H); 3.84 (br. *d*, *J*=6, 1 H); 5.50 (*d*, *J*=6, 1 H). ^{13}C-NMR: 16.6 (*q*); 18.8 (*t*); 21.6 (*t*); 27.6 (*q*); 29.8 (*q*); 30.0 (*d*); 33.1 (*q*); 36.2 (*s*); 37.3 (*t*); 39.7 (*s*); 42.1 (*t*); 45.9 (*d*); 57.3 (*t*); 71.0 (*d*); 116.7 (*d*); 157.0 (*s*). MS: 234 (14, M^+), 175 (46), 135 (39), 119 (41), 105 (88), 91 (56), 55 (55), 41 (100).

3-Methyl-1-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-1-ol (**13**). A soln. of β-cyclocitral (**12**; 10 g, 67 mmol) and 3-chloro-2-methylprop-1-ene (8.2 g, 91 mmol) in Et_2O (130 ml) was added dropwise during 75 min to a stirred slurry of Mg turnings (2.3 g, 95 mmol) in Et_2O (20 ml) containing MeI (50 mg) at reflux under N_2. After 2 h at reflux, the mixture was cooled to 5°, and sat. aq. NH_4Cl soln. (50 ml) was added dropwise. Extraction with Et_2O, workup, CC (cyclohexane/AcOEt 19:1), and bulb-to-bulb distillation *in vacuo* afforded **13** (12.7 g, 84%). Colorless oil. B.p. 120–130°/0.03 mbar. R_f 0.32 (cyclohexane/AcOEt 9:1). ^{1}H-NMR (after exchange with D_2O): 0.99 (*s*, 3 H); 1.12 (*s*, 3 H); 1.38–1.48 (*m*, 2 H); 1.50–1.61 (*m*, 2 H); 1.82 (*s*, 3 H); 1.85 (*s*, 3 H); 1.92–1.96 (*m*, 2 H); 2.17 (br. *d*, *J*=14, 1 H); 2.64 (*dd*, *J*=14, 11, 1 H); 4.40 (*dd*, *J*=11, 3, 1 H); 4.86 (*s*, 1 H); 4.90 (*s*, 1 H). ^{13}C-NMR: 19.4 (*t*); 21.1 (*q*); 22.3 (*q*); 28.1 (*q*); 28.7 (*q*); 34.1 (*t*); 34.8 (*s*); 40.1 (*t*); 45.2 (*t*); 68.3 (*d*); 113.1 (*t*); 131.5 (*s*); 139.1 (*s*); 143.7 (*s*). MS: 208 (<0.5, M^+), 153 (100), 119 (22), 109 (79), 95 (43), 69 (38).

4-{[(1,1-Dimethylethyl)(dimethyl)silyl]oxy}-2-methyl-4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-1-ene (**14**)[6]. A soln. of **13** (12.6 g, 55 mmol) in THF (20 ml) was added dropwise to a stirred slurry of NaH (60% suspension in oil; 2.8 g, 70 mmol) in THF (80 ml) at r.t. under N_2. The mixture was stirred at reflux during 7 h. Then, a soln. of *t*-Bu(Me_2)SiCl (TBDMSCl) (10.9 g, 70 mmol) in THF (20 ml) was added dropwise. After reflux for 2 h, the cooled mixture was poured into sat. aq. $NaHCO_3$ soln. and extracted with Et_2O. Workup, CC (cyclohexane/AcOEt 98:2), and distillation *in vacuo* afforded **14** (19.6 g, 83%). Colorless oil. B.p. 81–82°/0.02 Torr. R_f 0.74 (cyclohexane/AcOEt 9:1). IR ($CHCl_3$): 2930, 1472, 1375, 1082, 938, 835. ^{1}H-NMR: −0.04 (*s*, 3 H); 0.04 (*s*, 3 H); 0.85 (*s*, 9 H); 0.98 (*s*, 3 H); 1.13 (*s*, 3 H); 1.32–1.47 (*m*, 2 H); 1.50–1.60 (*m*, 2 H); 1.76 (*s*, 3 H); 1.83 (*s*, 3 H); 1.91 (*m*, 2 H); 2.15 (br. *d*, *J*=14, 1 H); 2.54 (*dd*, *J*=14, 11, 1 H); 4.37 (br. *d*, *J*=11, 1 H); 4.74 (br. *s*, 1 H); 4.76 (br. *s*, 1 H). ^{13}C-NMR: −4.8 (*q*); −4.3 (*q*); 18.4 (*s*); 19.4 (*t*); 21.5 (*q*); 22.5 (*q*); 26.0 (3*q*); 28.6 (*q*); 29.7 (*q*); 34.2 (*t*); 34.6 (*s*); 40.5 (*t*); 46.8 (*t*); 69.9 (*d*); 112.4 (*t*); 131.0 (*s*); 139.0 (*s*); 143.6 (*s*). MS: 322 (<0.5, M^+), 267 (27), 209 (3), 107 (8), 93 (9), 73 (100).

4-{[(1,1-Dimethylethyl)(dimethyl)silyl]oxy}-2-methyl-4-(2,6,6-trimethylcyclohex-1-en-1-yl)butan-1-ol (**15**). A soln. of 9-borabicyclo[3.3.1]nonane (9-BBN; 70 mmol) in THF (140 ml) was added dropwise during 1 h to a stirred soln. of **14** (19.5 g, 45 mmol) in THF (80 ml) at r.t. under N_2. After 5 h, the mixture was cooled to −5°, and 3N aq. NaOH soln. (32 ml) was added dropwise, followed by 35% aq. H_2O_2 soln. (32 ml). The mixture was stirred at 45° over 45 min, poured into H_2O, and extracted with Et_2O. The org. phase was washed with 5% aq. HCl soln. and brine. Workup, CC (cyclohexane/AcOEt 9:1), and bulb-to-bulb distillation *in vacuo* afforded **15** as a 1.4:1 diastereoisomer mixture (13.0 g, 78%). Colorless oil. B.p. 200–210°/0.04 mbar. Samples of the pure diastereoisomers were obtained by repeated CC (cyclohexane/AcOEt 94:6).

Data of Major Diastereoisomer of **15**. R_f 0.26 (cyclohexane/AcOEt 9:1). IR ($CHCl_3$): 3620, 3500 (br.), 2930, 1472, 1255, 1076, 836. ^{1}H-NMR (after exchange with D_2O): 0.00 (*s*, 3 H); 0.10 (*s*, 3 H); 0.91 (*s*, 9 H); 0.96 (*s*, 3 H); 1.00 (*d*, *J*=7, 3 H); 1.13 (*s*, 3 H); 1.30–1.60 (*m*, 6 H); 1.83 (*s*, 3 H); 1.78–2.05 (*m*, 3 H); 3.49 (*dd*, *J*=11, 7, 1 H); 3.65 (*dd*, *J*=11, 4, 1 H); 4.33 (*dd*, *J*=11, 7, 1 H). ^{13}C-NMR: −4.9 (*q*); −4.1 (*q*); 18.3 (*q*); 18.3 (*s*); 19.4 (*t*); 21.7 (*q*); 26.0 (3*q*); 28.5 (*q*); 29.7 (*q*); 32.8 (*d*); 34.2 (*t*); 34.5 (*s*); 40.5 (*t*); 42.0 (*t*); 66.9 (*t*); 69.7 (*d*); 131.0 (*s*); 139.1 (*s*). MS: 340 (<0.5, M^+), 267 (18), 227 (49), 135 (20), 107 (27), 93 (28).

Data of Minor Diastereoisomer of **15**. R_f 0.22 (cyclohexane/AcOEt 9:1). IR ($CHCl_3$): 3620, 3480 (br.), 2930, 1472, 1256, 1074, 836. ^{1}H-NMR (after exchange with D_2O): 0.00 (*s*, 3 H); 0.11 (*s*, 3 H); 0.90 (*s*, 9 H); 0.95 (*s*, 3 H); 0.97 (*d*, *J*=7, 3 H); 1.14 (*s*, 3 H); 1.14–1.24 (*m*, 1 H); 1.33–1.48 (*m*, 2 H); 1.52–1.60 (*m*, 2 H); 1.82 (*s*, 3 H); 1.85–2.05 (*m*, 4 H); 3.43–3.53 (*m*, 2 H); 4.34 (br. *d*, *J*=11, 1 H).

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[6]) Systematic name: (1,1-dimethylethyl)(dimethyl){[3-methyl-1-(2,6,6-trimethylcyclohex-1-en-1-yl)-but-3-en-1-yl]oxy}silane.

^{13}C-NMR: −5.0 (*q*); −4.1 (*q*); 15.7 (*q*); 18.4 (*s*); 19.4 (*t*); 21.7 (*q*); 26.0 (3*q*); 28.5 (*q*); 29.8 (*q*); 33.1 (*d*); 34.2 (*t*); 34.6 (*s*); 40.5 (*t*); 41.9 (*t*); 69.2 (*t*); 69.2 (*d*); 131.1 (*s*); 138.9 (*s*). MS: 340 (<0.5, M^+), 267 (15), 227 (48), 135 (20), 107 (25), 93 (29), 75 (100).

4-{[(1,1-Dimethylethyl)(dimethyl)silyl]oxy}-2-methyl-4-(2,6,6-trimethylcyclohex-1-en-1-yl)butanal (**16**). DMSO (7.4 ml, 45 mmol) in CH_2Cl_2 (25 ml) was added dropwise to a stirred soln. of oxalyl chloride (4.4 ml, 51 mmol) in CH_2Cl_2 (100 ml) at −55° under N_2. After 2 min, a soln. of **15** (1.4:1 diastereoisomer mixture; 12.9 g, 35 mmol) in CH_2Cl_2 (20 ml) was added dropwise over 15 min at −55°. After a further 15 min, CH_2Cl_2 (60 ml) was added, followed by Et_3N (12.5 ml, 90 mmol). After 5 min, the mixture was allowed to attain r.t. over 1 h. Brine was added, and the mixture was extracted with CH_2Cl_2. The org. phase was washed successively with cold 5% aq. HCl and brine. Workup, CC (cyclohexane/AcOEt 19:1), and bulb-to-bulb distillation *in vacuo* afforded **16** as a 1.4:1 diastereoisomer mixture (10.2 g, 85%). Colorless oil. B.p. 190–200°/0.04 mbar. Samples of the pure diastereoisomers were obtained by CC (cyclohexane/AcOEt 98:2).

Data of Major Diastereoisomer of **16**. R_f 0.47 (cyclohexane/AcOEt 19:1). IR ($CHCl_3$): 2931, 1721, 1256. ^{1}H-NMR: −0.03 (*s*, 3 H); 0.05 (*s*, 3 H); 0.89 (*s*, 9 H); 0.99 (*s*, 3 H); 1.10 (*s*, 3 H); 1.13 (*d*, *J*=7, 3 H); 1.32–1.48 (*m*, 2 H); 1.50–1.59 (2 H); 1.82 (*s*, 3 H); 1.80–2.00 (*m*, 4 H); 2.67–2.79 (*m*, 1 H); 4.29 (*dd*, *J*=11, 3, 1 H); 9.70 (*d*, *J*=3, 3 H). ^{13}C-NMR: −5.0 (*q*); −4.1 (*q*); 14.6 (*q*); 18.4 (*s*); 19.3 (*t*); 21.6 (*q*); 26.0 (3 *q*); 28.4 (*q*); 29.8 (*q*); 34.2 (*t*); 34.5 (*s*); 40.0 (*t*); 40.5 (*t*); 43.7 (*d*); 69.2 (*d*); 131.4 (*s*); 138.7 (*s*); 205.2 (*d*). MS: 338 (<0.5, M^+), 281 (7), 149 (6), 119 (25), 107 (23), 93 (23), 75 (100).

Data of Minor Diastereoisomer of **16**. R_f 0.33 (cyclohexane/AcOEt 19:1). IR ($CHCl_3$): 2931, 1719, 1719, 1472, 1217, 1085, 836. ^{1}H-NMR: 0.00 (*s*, 3 H); 0.10 (*s*, 3 H); 0.89 (*s*, 9 H); 0.94 (*s*, 3 H); 1.12 (*d*, *J*=7, 3 H); 1.14 (*s*, 3 H); 1.27–1.49 (*m*, 3 H); 1.50–1.61 (*m*, 2 H); 1.84 (*s*, 3 H); 1.87–2.01 (*m*, 2 H); 2.31–2.41 (*m*, 1 H); 2.64–2.76 (*m*, 1 H); 4.33 (*dd*, *J*=11, 3, 1 H); 9.69 (*d*, *J*=1.5, 1 H). ^{13}C-NMR: −5.0 (*q*); −4.2 (*q*); 12.1 (*q*); 18.4 (*s*); 19.3 (*t*); 21.7 (*q*); 26.0 (3 *q*); 28.5 (*q*); 29.8 (*q*); 34.2 (*t*); 34.6 (*s*); 38.4 (*t*); 40.4 (*t*); 44.2 (*d*); 68.5 (*d*); 132.0 (*s*); 138.1 (*s*); 205.2 (*d*). MS: 338 (<0.5, M^+), 281 (7), 149 (20), 119 (30), 107 (28), 93 (27), 75 (100).

Methyl 6-{[(1,1-Dimethylethyl)(dimethyl)silyl]oxy}-4-methyl-6-(2,6,6-trimethylcyclohex-1-en-1-yl)hex-2-enoate (**17**). A soln. of MeONa (*ca.* 5.4M in MeOH; 5.1 ml, 28 mmol) in MeOH (10 ml) was added dropwise during 15 min to a stirred mixture of **16** (7.7 g, 22 mmol) and trimethylphosphonoacetate (5.8 g, 32 mmol) in toluene (40 ml) at 3 to 6° under N_2. The mixture was allowed to attain r.t. during 30 min, stirred for a further 1 h, and then poured into cold 10% aq. NH_4Cl soln. Extraction with (Et_2O), workup, and concentration *in vacuo* afforded crude **17** (9.5 g, 93%) as a pale-yellow oil consisting of an (*E*/*Z*) 81:19 mixture. An anal. sample (160 mg) was subjected to CC (cyclohexane/AcOEt 98:2), which afforded the more-polar (*E*)-**17** and the less-polar (*Z*)-**17** isomers, both as 1.2:1 diastereoisomer mixtures.

Data of (*E*)-**17** (1.2:1 diastereoisomer mixture). ^{1}H-NMR: −0.05, −0.02 (2*s*, 3 H); 0.05, 0.08 (2*s*, 3 H); 0.89, 0.88 (2*s*, 9 H); 0.87, 0.92 (2*s*, 3 H); 1.06 (2*d*, *J*=7, 3 H); 1.06, 1.12 (2*s*, 3 H); 1.78 (2*s*, 3 H); 2.61–2.73 (*m*, 1 H); 3.74, 3.71 (2*s*, 3 H); 4.10, 4.31 (2 br. *d*, *J*=9, 1 H); 5.84, 5.78 (2*d*, *J*=15, 1 H); 6.84, 6.97 (2*dd*, *J*=15, 6, 1 H). ^{13}C-NMR: −5.0, −4.9 (2*q*); −4.1, −4.0 (2*q*); 16.8 (2*d*); 18.4 (2*s*); 19.4 (2*t*); 21.1, 21.7 (2*q*); 26.0, 26.1 (2*q*); 28.4, 28.5 (2*q*); 29.8, 29.9 (2*q*); 33.0, 34.2 (2*d*); 34.2 (2*t*); 34.6, 34.7 (2*s*); 40.4, 40.5 (2*t*); 43.9, 45.3 (2*t*); 51.5 (2*q*); 68.4, 69.4 (2*d*); 118.3, 120.4 (2*d*); 131.2, 131.6 (2*s*); 138.4, 138.7 (2*s*); 154.5, 155.8 (2*d*); 167.4, 167.6 (2*s*). MS: 394 (<0.55, M^+), 337 (66), 267 (100), 199 (15), 75 (76).

Data of (*Z*)-**17** (1.2:1 diastereoisomer mixture). ^{1}H-NMR: −0.07, −0.02 (2*s*, 3 H); −0.02, 0.08 (2*s*, 3 H); 0.87, 0.90 (2*s*, 9 H); 0.95 (2*s*, 3 H); 1.06, 1.03 (2*d*, *J*=7, 3 H); 1.08, 1.11 (2*s*, 3 H); 1.79 (2*s*, 3 H); 3.57–3.67 (*m*, 1 H); 3.69, 3.70 (2*s*, 3 H); 4.08, 4.31 (2 br. *d*, *J*=9, 1 H); 5.65, 5.78 (2*d*, *J*=10, 1 H); 6.03, 6.07 (2*dd*, *J*=10, 8, 1 H). ^{13}C-NMR: −5.2, −4.9 (2*q*); −4.1, −4.0 (2*q*); 18.3 (2*s*); 18.7 (2*d*); 19.4 (2*t*); 21.2, 21.7 (2*q*); 26.1, 26.2 (2*q*); 28.4, 28.5 (2*q*); 29.8, 30.0 (2*q*); 30.7, 31.3 (2*d*); 34.2 (2*t*); 34.7 (2*s*); 40.5 (2*t*); 45.0, 46.7 (2*t*); 51.1, 51.2 (2*q*); 69.0, 70.1 (2*d*); 117.5, 119.3 (2*d*); 131.0, 131.2 (2*s*); 138.9, 139.0 (2*s*); 155.8, 156.0 (2*d*); 166.6, 166.9 (2*s*). MS: 394 (<0.5, M^+), 337 (76), 267 (100), 199 (12), 75 (72).

Methyl 6-{[(1,1-Dimethylethyl)(dimethyl)silyl]oxy}-4-methyl-6-(2,6,6-trimethylcyclohex-1-en-1-yl)-hex-3-enoate (**18**). A soln. of **17** ((*E*/*Z*) 81:19; 9.3 g, 20 mmol) in 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 50 ml) was heated at 95–98° during 5 h under N_2. The cooled mixture was poured into cold aq. HCl soln. (120 ml) and extracted with Et_2O. Workup and concentration *in vacuo* afforded a pale-yellow oil (8.8 g), which, according to GC analysis, contained a mixture of **17** ((*E*/*Z*) 3:1; 24%) and **18** ((*E*/

Z) 1.9:1; 72%). Purification of an aliquot (200 mg) by CC (cyclohexane/AcOEt 98.5:1.5) afforded pure samples of the more polar (*E*)- and the less polar (*Z*)-isomer of **18**.

Data of (*E*)-**18**. ^{1}H-NMR: −0.05 (*s*, 3 H); −0.01 (*s*, 3 H); 0.82 (*s*, 9 H); 0.97 (*s*, 3 H); 1.11 (*s*, 3 H); 1.67 (*s*, 3 H); 1.81 (*s*, 3 H); 2.19 (br. *d*, *J* = 12, 1 H); 2.52 (*dd*, *J* = 12, 8, 1 H); 2.96–3.13 (*m*, 2 H); 3.67 (*s*, 3 H); 4.30–4.40 (*m*, 1 H); 5.39 (br. *t*, *J* = 6, 1 H). ^{13}C-NMR: −4.9 (*q*); −4.3 (*q*); 16.4 (*q*); 18.3 (*s*); 19.4 (*t*); 21.6 (*q*); 25.9 (3*q*); 28.6 (*q*); 29.7 (*q*); 33.8 (*t*); 34.2 (*t*); 34.6 (*s*); 40.5 (*t*); 48.2 (*t*); 51.6 (*q*); 69.6 (*d*); 118.1 (*d*); 131.2 (*s*); 136.9 (*s*); 138.8 (*s*); 172.7 (*s*). MS: 394 (< 0.5, M^+), 267 (100), 185 (11), 75 (17), 73 (27).

Data of (*Z*)-**18**. ^{1}H-NMR: −0.03 (*s*, 3 H); −0.01 (*s*, 3 H); 0.81 (*s*, 9 H); 0.97 (*s*, 3 H); 1.11 (*s*, 3 H); 1.79 (*s*, 3 H); 1.87 (*s*, 3 H); 2.77 (*dd*, *J* = 12, 9, 1 H); 3.03–3.11 (*m*, 1 H); 3.18–3.26 (*m*, 1 H); 3.68 (*s*, 3 H); 4.39–4.43 (*m*, 1 H); 5.40 (br. *t*, *J* = 6, 1 H). ^{13}C-NMR: −4.8 (*q*); −4.3 (*q*); 18.4 (*s*); 19.4 (*t*); 21.7 (*q*); 23.3 (*q*); 25.9 (3*q*); 28.7 (*q*); 29.7 (*q*); 33.7 (*t*); 34.2 (*t*); 34.6 (*s*); 40.5 (*t*); 40.7 (*t*); 51.8 (*q*); 69.2 (*d*); 118.3 (*d*); 131.4 (*s*); 137.0 (*s*); 138.9 (*s*); 173.1 (*s*). MS: 394 (< 0.5, M^+), 267 (100), 185 (4), 75 (17), 73 (23).

6-{[(1,1-Dimethylethyl)(dimethyl)silyl]oxy}-4-methyl-6-(2,6,6-trimethylcyclohex-1-en-1-yl)hex-3-en-1-ol (**19**). A soln. of **18** ((*E*/*Z*) 1.9:1; 8.6 g, 15 mmol) in THF (40 ml) was added dropwise during 10 min to a stirred slurry of $LiAlH_4$ (0.6 g, 15 mmol) in THF (20 ml) at 25–40° under N_2. After reflux for 1 h, the cooled mixture was treated with H_2O (0.6 ml), and further THF (20 ml) was added. Subsequently, 15% aq. NaOH soln. (0.6 ml) was added cautiously, and, after stirring for a further 10 min, more H_2O (1.6 ml) was added. Stirring at r.t. for 45 min was followed by filtration through *Celite*. Concentration *in vacuo* gave a yellow viscous oil (7.6 g), which was purified by CC (cyclohexane/AcOEt 95:5) and bulb-to-bulb distillation (200–210°/0.05 mbar) to afford **19** ((*E*/*Z*) 2.5:1) as a pale-yellow oil (5.7 g, 88%). An aliquot (200 mg) was subjected to CC (cyclohexane/AcOEt 9:1), which afforded pure (*E*)- and (*Z*)-**19**.

Data of (*E*)-**19**. R_f 0.21 (cyclohexane/AcOEt 9:1). IR ($CHCl_3$): 3640, 2930, 1472, 1255, 1081, 837. ^{1}H-NMR (after exchange with D_2O): −0.05 (*s*, 3 H); 0.00 (*s*, 3 H); 0.84 (*s*, 9 H); 0.97 (*s*, 3 H); 1.11 (*s*, 3 H); 1.32–1.46 (*m*, 2 H); 1.49–1.60 (*m*, 2 H); 1.68 (*s*, 3 H); 1.82 (*s*, 3 H); 1.78–1.88 (*m*, 2 H); 2.17 (br. *d*, *J* = 14, 1 H); 2.15–2.40 (*m*, 2 H); 2.50 (*dd*, *J* = 14, 11, 1 H); 3.57–3.69 (*m*, 2 H); 4.35 (br. *d*, *J* = 11, 1 H); 5.18 (br. *t*, *J* = 7, 1 H). ^{13}C-NMR: −4.8 (*q*); −4.2 (*q*); 16.4 (*q*); 18.3 (*s*); 19.4 (*t*); 21.6 (*q*); 26.0 (3*q*); 28.7 (*q*); 29.7 (*q*); 31.8 (*t*); 34.2 (*t*); 34.6 (*s*); 40.6 (*t*); 48.6 (*t*); 62.5 (*t*); 69.8 (*d*); 122.3 (*d*); 131.1 (*s*); 136.6 (*s*); 139.0 (*s*). MS: 366 (< 0.5, M^+), 267 (13), 135 (14), 93 (9), 73 (100).

Data of (*Z*)-**19**. R_f 0.25 (cyclohexane/AcOEt 9:1). IR ($CHCl_3$): 3620, 3460 (br.), 2930, 1472, 1377, 1255, 1078, 937. ^{1}H-NMR (after exchange with D_2O): −0.02 (*s*, 3 H); 0.03 (*s*, 3 H); 0.83 (*s*, 9 H); 0.98 (*s*, 3 H); 1.12 (*s*, 3 H); 1.33–1.46 (*m*, 2 H); 1.50–1.60 (*m*, 2 H); 1.78 (*s*, 3 H); 1.87 (*s*, 3 H); 1.80–2.02 (*m*, 2 H); 1.98 (br. *d*, *J* = 14, 1 H); 2.23–2.47 (*m*, 2 H); 2.86 (*dd*, *J* = 14, 11, 1 H); 3.56–3.67 (*m*, 2 H); 4.44 (*dd*, *J* = 11, 3, 1 H); 5.20 (br. *t*, *J* = 7, 1 H). ^{13}C-NMR: −4.7 (*q*); −4.3 (*q*); 18.4 (*s*); 19.4 (*t*); 21.7 (*q*); 23.4 (*q*); 26.0 (3*q*); 28.7 (*q*); 29.7 (*q*); 31.7 (*t*); 34.3 (*t*); 34.5 (*s*); 40.4 (*t*); 40.6 (*t*); 62.7 (*t*); 69.4 (*d*); 122.7 (*d*); 131.4 (*s*); 136.7 (*s*); 139.1 (*s*). MS: 366 (< 0.5, M^+), 267 (28), 135 (4), 93 (10), 73 (100).

4-Methyl-6-(2,6,6-trimethylcyclohex-1-en-1-yl)hex-3-en-1,6-diol (**3**). A mixture of **19** ((*E*/*Z*) 2.5:1; 5.5 g, 13 mmol) and tetrabutylammonium fluoride trihydrate (TBAF; 8.5 g, 27 mmol) in THF (60 ml) was heated at reflux during 3 d under N_2. The cooled mixture was poured into H_2O and extracted with Et_2O. Workup and concentration *in vacuo* afforded crude **3** (3.9 g, 87%; (*E*/*Z*) 2.5:1) as a yellow oil. Purification by CC (cyclohexane/AcOEt 60:40) and recrystallization (pentane/Et_2O 9:1) afforded the pure, more polar (*E*)-**3** (2 g) and the less-polar (*Z*)-**3** (0.9 g) isomers.

Data of (*E*)-**3**. M.p. 94–95°. IR ($CHCl_3$): 3422 (br.), 2932, 1385, 1047. ^{1}H-NMR (after exchange with D_2O): 0.99 (*s*, 3 H); 1.11 (*s*, 3 H); 1.38–1.46 (*m*, 2 H); 1.51–1.61 (*m*, 2 H); 1.74 (*s*, 3 H); 1.84 (*s*, 3 H); 1.90–1.98 (*m*, 2 H); 2.19 (br. *d*, *J* = 14, 1 H); 2.25–2.43 (*m*, 2 H); 2.60 (*dd*, *J* = 14, 11, 1 H); 3.60–3.70 (*m*, 2 H); 4.37 (*dd*, *J* = 11, 3, 1 H); 5.30 (br. *t*, *J* = 7, 1 H). ^{13}C-NMR: 16.2 (*q*); 19.4 (*t*); 21.2 (*q*); 28.2 (*q*); 28.7 (*q*); 31.5 (*t*); 34.2 (*t*); 34.8 (*s*); 40.1 (*t*); 46.9 (*t*); 62.1 (*t*); 68.1 (*d*); 123.8 (*d*); 131.5 (*s*); 136.3 (*s*); 139.3 (*s*). MS: 252 (< 0.5, M^+), 153 (100), 109 (71), 95 (44), 69 (42).

Data of (*Z*)-**3**. M.p. 72–73°. ^{1}H-NMR (after exchange with D_2O): 1.00 (*s*, 3 H); 1.11 (*s*, 3 H); 1.88–2.00 (*m*, 2 H); 1.52–1.60 (*m*, 2 H); 1.73 (*s*, 3 H); 1.91 (2*s*, 6 H); 2.18–2.27 (*m*, 1 H); 2.45–2.56 (*m*, 1 H); 3.05 (*dd*, *J* = 12, 10, 1 H); 3.55–3.61 (*m*, 1 H); 3.69–3.74 (*m*, 1 H); 4.44 (*dd*, *J* = 10, 2, 1 H); 5.30–5.37 (*m*, 1 H). ^{13}C-NMR: 19.3 (*t*); 21.2 (*q*); 23.6 (*q*); 28.1 (*q*); 28.7 (*q*); 31.4 (*t*); 34.1 (*t*); 34.8 (*s*); 38.6 (*t*); 40.0 (*t*); 62.0 (*t*); 68.3 (*d*); 124.8 (*d*); 131.5 (*s*); 135.7 (*s*); 139.6 (*s*). MS: 252 (< 0.5, M^+), 234 (17), 153 (100), 109 (49).

Acid-Mediated Cyclization of (*E*)-**3**. A soln. of (*E*)-**3** (0.4 g, 1.57 mmol) in CH_2Cl_2 (5 ml) was added to a mechanically stirred soln. of CF_3CO_2H (4 ml, 51 mmol) in CH_2Cl_2 (35 ml) at $-15°$ under N_2. The color gradually changed to yellow and then to orange. After a further 45 min at $-10°$, sat. aq. Na_2CO_3 soln. (40 ml) was rapidly added dropwise (temperature rise to 10°). Extraction with Et_2O, workup, and concentration *in vacuo* gave a yellow viscous oil (390 mg), which was filtered over silica gel, eluting with cyclohexane/AcOEt 95:5, to afford, after bulb-to-bulb distillation (160–170°/0.03 mbar), a colorless oil (142 mg, 35%). The oil was shown by GC analysis to consist of four major products: **1c** (45%), **1d** (34%), **1b** (2%), and *2-methyl-2-[(*E*)-2-(2,6,6-trimethylcyclohex-1-en-1-yl)ethenyl]tetrahydrofuran* (**21**; 19%). The latter compound was isolated by CC (cyclohexane/AcOEt 98:2).

Data of **21**. IR ($CHCl_3$): 2968, 1458, 1029. ^{1}H-NMR: 0.98 (*s*, 6 H); 1.36 (*s*, 3 H); 1.42–1.47 (*m*, 2 H); 1.55–1.75 (*m*, 4 H); 1.65 (*s*, 3 H); 1.90–2.00 (*m*, 4 H); 3.85–3.95 (*m*, 2 H); 5.40 (*d*, $J=16$, 1 H); 6.00 (br. *d*, $J=16$, 1 H). MS: 234 (22, M^+), 219 (43), 119 (41), 105 (69), 98 (58), 85 (61), 71 (66), 43 (100).

Acid-Mediated Cyclization of (*Z*)-**3**. A soln. of (*Z*)-**3** (0.4 g, 1.57 mmol) in CH_2Cl_2 (5 ml) was submitted to the same cyclization conditions and workup as described above to afford a colorless oil (150 mg, 37%) consisting of **1a** (50%), **1b** (36%), **1d** (1%), and **21** (13%), which were identical to authentic samples (*vide supra*).

Acid-Mediated Cyclization of **10**. Using the same procedure as described for the cyclizations of (*E*)-**2** and (*Z*)-**2** (*vide supra*), compound **10** (1:1 diastereoisomer mixture; 1.3 g, 5.3 mmol) was treated with $ClSO_3H$ (2 ml, 30 mmol) at $-80°$ to afford, after CC (cyclohexane/AcOEt 19:1) and bulb-to-bulb distillation *in vacuo* (140–150°/0.04 mbar), a 10:1 mixture of **22a** and **22b** (330 mg, 27%). Repeated CC (cyclohexane/AcOEt 19:1) allowed the isolation of samples (*ca.* 40 mg) of **22a** and **22a**/**22b** (*ca.* 1:1).

Data of (*3a*RS,*9a*RS)*-2,3a,4,6,7,8,9,9a-Octahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan* (**22a**). R_f 0.36 (cyclohexane/AcOEt 9:1). GC: t_R 3.22. IR: 2926, 1464, 1363, 1296, 1206, 1139, 1084, 1060, 1040, 1025. ^{1}H-NMR: 1.07 (*s*, 3 H); 1.15 (*s*, 3 H); 1.38 (*s*, 3 H); 1.43 (*s*, 3 H); 1.20–1.70 (4 H); 1.77–1.92 (*m*, 2 H); 2.20–2.38 (*m*, 2 H); 4.56 (*dd*, $J=12$, 2, 1 H); 4.66 (br. *d*, $J=12$, 1 H); 5.46 (br. *s*, 1 H); 5.59 (*dd*, $J=7$, 3.5, 1 H). ^{13}C-NMR: 19.4 (*t*, C(8)); 24.4 (*q*, Me–C(3a)); 28.4 (*q*, Me–C(9a)); 29.3 (*q*, Me_β–C(6)); 33.7 (*q*, Me_α–C(6)); 35.9 (*s*, C(6)); 39.3 (*t*, C(4)); 40.1 (*s*, C(9a)); 40.3 (*t*, C(9)); 41.2 (*t*, C(7)); 73.0 (*t*, C(2)); 86.9 (*s*, C(3a)); 116.1 (*d*, C(1)); 118.4 (*d*, C(5)); 148.8 (*s*, C(5a)); 155.2 (*s*, C(9b)). MS: 232 (11, M^+), 217 (100), 175 (8), 147 (23), 119 (12), 91 (14), 43 (32).

*Data of (3a*RS,*9a*SR*)-2,3a,4,6,7,8,9,9a-Octahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan* (**22b**). R_f 0.37 (cyclohexane/AcOEt 9:1). GC: t_R 3.53. ^{1}H-NMR: 1.12 (*s*, 3 H); 1.18 (*s*, 3 H); 1.30 (*s*, 3 H); 1.40 (*s*, 3 H); 1.20–1.70 (4 H); 1.82–1.96 (*m*, 2 H); 2.31–2.41 (*m*, 2 H); 4.53 (*dd*, $J=12$, 2, 1 H); 4.66 (br. *d*, $J=12$, 1 H); 5.28 (br. *s*, 1 H); 5.43 (*dd*, $J=6$, 3.5, 1 H). ^{13}C-NMR: 18.5 (*t*, C(8)); 27.2 (*q*, Me–C(9a)); 27.4 (*q*, Me–C(3a)); 28.8 (*q*, Me_β–C(6)); 33.0 (*q*, Me_α–C(6)); 36.5 (*s*, C(6)); 38.8 (*s*, C(9a)); 39.1 (*s*, C(9)); 41.8 (*t*, C(7)); 42.0 (*t*, C(4)); 72.8 (*t*, C(2)); 85.4 (*s*, C(3a)); 112.8 (*d*, C(1)); 117.4 (*d*, C(5)); 147.4 (*s*, C(5a)); 154.3 (*s*, C(9b)). MS: 232 (10, M^+), 217 (100), 175 (9), 147 (22), 119 (11), 91 (13), 43 (27).

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