Internal Nucleophilic Termination in Acid-Mediated Polyene Cyclizations

Part 3[1])

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

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Dedicated to Dr. *Günther Ohloff* on the occasion of his 80th birthday

Treatment of the unsaturated allenic alcohols (*E*)-**7**, (*Z*)-**7**, **10**, **13**, and **19** with an excess of FSO_3H in 2-nitropropane at −90° to −30° afforded, in 68–85% yield, diastereoisomer mixtures of racemic tricyclic ethers **14a–d** and **20a–d**, respectively (*Schemes 3* and *5*), with high stereoselectivity (see *Table* and *Scheme 6*). These stereospecific transformations represent the first reported examples of an acid-mediated polyene cyclization, in which an alkene is the initiating group and an allenic alcohol serves as the internal terminator. In close analogy to our earlier work, a nonsynchronous process is postulated, whereby the stereochemical course of cyclization is directed by the conformational structure of an intermediate cyclohexyl cation (see *Schemes 3* and *6*). In addition, the organoleptic properties of **14c** and **20c**, racemic didehydro and methyl didehydro analogues, respectively, of the known odorant *Ambrox*® ((−)-**4f**), are briefly discussed.

1. Introduction. – With the aim to find efficient routes to organoleptically active tricyclic ethers possessing the labdane skeleton, we described in 1992 stereoselective syntheses of racemic *Ambrox*® (**4f**)[2]) and of three of its diastereoisomers (see **4c**, **4g**, and **4d**)[3]) from the appropriate unsaturated acyclic (see **1**) or monocyclic (see **2** and **3**) homoallylic alcohol, by using an excess of fluorosulfuric acid (FSO_3H) in 2-nitropropane at −90° [1] (*Scheme 1*). These stereospecific reactions represent rare examples of acid-mediated polyene cyclizations in which the initiating group is an alkene and where termination is effected internally by an OH group[4]).

Subsequent work [2], involving the cyclization of Me-substituted analogues of **2** and **3** (Me groups at C(1) and C(5′)), reinforced our mechanistic hypothesis and demonstrated that the efficiency of this reaction is independent of the nature of the OH group, which may be primary, secondary, or tertiary. In continuation of our studies, we now report the acid-mediated cyclizations of a series of unsaturated allenic alcohols.

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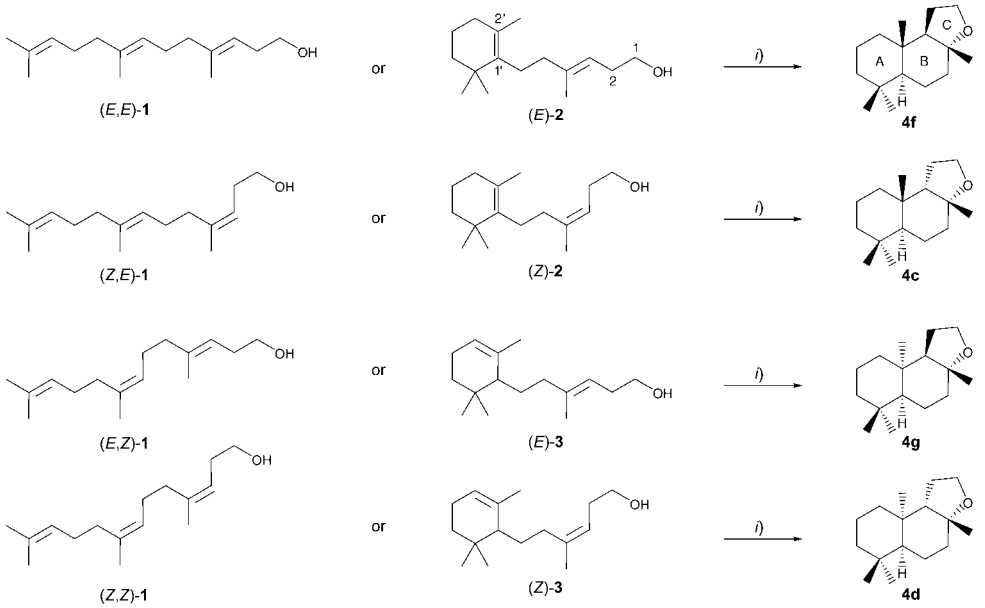
[1]) For Parts 1 and 2, see [1] and [2], resp.

[2]) *Ambrox*® ((−)-**4f**; trade name of *Firmenich SA*) is a commercially important, naturally occurring odorant, see [3][4]; the racemate **4f** is commercialized by *Firmenich SA* under the trade name *Cetalox*® [5].

[3]) For the synthesis and spectral characterization of all seven diastereoisomers **4a–g**, see [6]; the letters **a–g** reflect the GC elution order (lower to higher retention times), the same convention being applied for **14a–d** and **20a–d** (see *Exper. Part*).

[4]) For related independent studies, see [7]; for a recent *Lewis* acid mediated asymmetric cyclization of (*E*,*E*)-**1** to **4f**, see [8]; for an enzymatic cyclization of the same substrate with squalene cyclase, see [9].

Scheme 1



i) FSO_3H (10 mol-equiv.), 2-nitropropane, $-90°$ (yield: 40–80%).

Our interest was twofold. First, allenic alcohols have never been reported as terminating groups in polyene cyclizations. Second, if successful, this reaction would offer an efficient access to novel 1,9b-didehydro analogues of **4**, whose organoleptic properties would be of special interest with regard to structure–activity studies [10][5]).

2. Results and Discussion. – 2.1. *Allenic Alcohols* (E)-**7**, *(Z)*-**7**, **10**, *and* **13**. Configurationally pure samples of the four racemic allenic alcohols (*E*)- and (*Z*)-**7**, **10**, and **13**[6]) were prepared from ketones (*E*)- and (*Z*)-**5**, **8**, and **11**, respectively, by using a modified published methodology [12]. This four-step procedure (overall yield *ca.* 40–60%; see *Scheme 2*) involves: *i*) base-mediated 1,2-addition of prop-2-yn-1-ol, affording diols (*E*)- and (*Z*)-**6a**, **9a**, and **12a**, respectively; *ii*) selective acetylation of the primary OH group to (*E*)- and (*Z*)-**6b**, **9b**, and **12b**, respectively; *iii*) protection of the tertiary OH group *via* acetal formation by using the acid-catalyzed addition of ethyl vinyl ether[7]) without isolation of the doubly protected diol intermediate; and *iv*) treatment with $LiAlH_4$ for deprotection of the primary OH group, and concomitant internal hydride displacement of the *O*-(1-ethoxyethyl) group.

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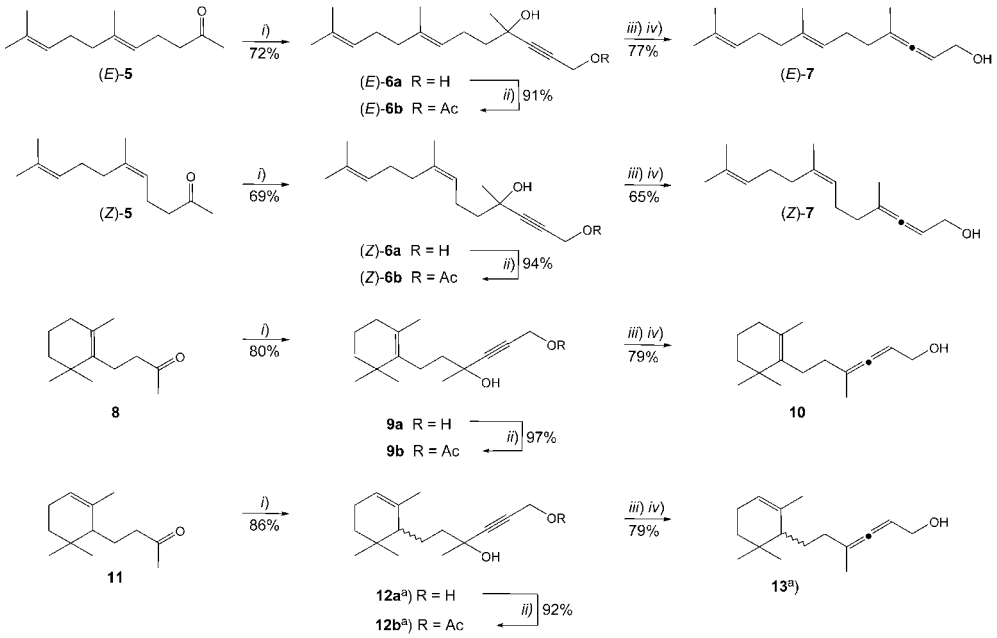
5) Part of this work has already been described in a *Firmenich* patent, see [11].

6) All chiral compounds synthesized in this work are racemic.

7) The use of ethyl vinyl ether, as opposed to the reported 3,4-dihydro-2*H*-pyran [12], affords higher yields of the allenic alcohols.

Scheme 2



[a]) 1:1 mixture of diastereoisomers.

i) Prop-2-yn-1-ol, KOH, THF, r.t. *ii*) Ac_2O, Et_3N, r.t. *iii*) Ethyl vinyl ether, cat. $TsOH \cdot H_2O$, toluene, $-20°$. *iv*) $LiAlH_4$, THF, toluene, r.t.

2.2. *Acid-Mediated Cyclization* (FSO_3H/2-nitropropane) *of* (E)-**7**, *(Z)*-**7**, **10**, *and* **13** *to Tricyclic Ethers* **14a**–**d**. The acid-mediated cyclizations of (*E*)- and (*Z*)-**7**, **10**, and **13** were effected by treatment of each substrate with an excess of FSO_3H (2.3 mol-equiv.) in 2-nitropropane at $-90°$ to $-30°$ during 1 h (*Scheme 3*). Subsequent neutralization with aqueous $NaHCO_3$ solution, extractive workup, and distillation *in vacuo* afforded mixtures of **14a**–**d** in 68–85% yield; the product distributions, determined by anal. GC, are presented in the *Table*. Pure samples of each of the four diastereoisomers were obtained by a combination of column chromatography and prep. GC, and fully characterized spectroscopically. Structural attributions were established by inspection of the NMR spectra, and corroborated by catalytic hydrogenation to the dihydro analogs **4a**–**d**, which were identified by GC and spectral comparison with authentic samples [6][8]).

A mechanistic rationale for the observed results, analogous to our earlier work [1][2], is presented in *Scheme 3*. The observation that cyclization of either (*E*)-**7** or **10** (*Table*, *Entries 1* and *3*) gives **14c** as the major product (88% and 84% selectivity, resp.), whereas (*Z*)-**7** or **13** (*Entries 2* and *5*) predominantly afford **14b** (83%

[8]) It is interesting to note that, whereas **14a**, **14c**, and **14d** were almost completely hydrogenated to **4a**, **4c**, and **4d**, resp., **14b** underwent only partial conversion (*ca.* 15%) to **4b** (for details, see *Exper. Part.*).

Scheme 3. *Acid-Mediated Cyclizations of* (E)- *and* (Z)-**7**, **10**, *and* **13**: *Mechanitic Rationale for Formation of* **14a – d**

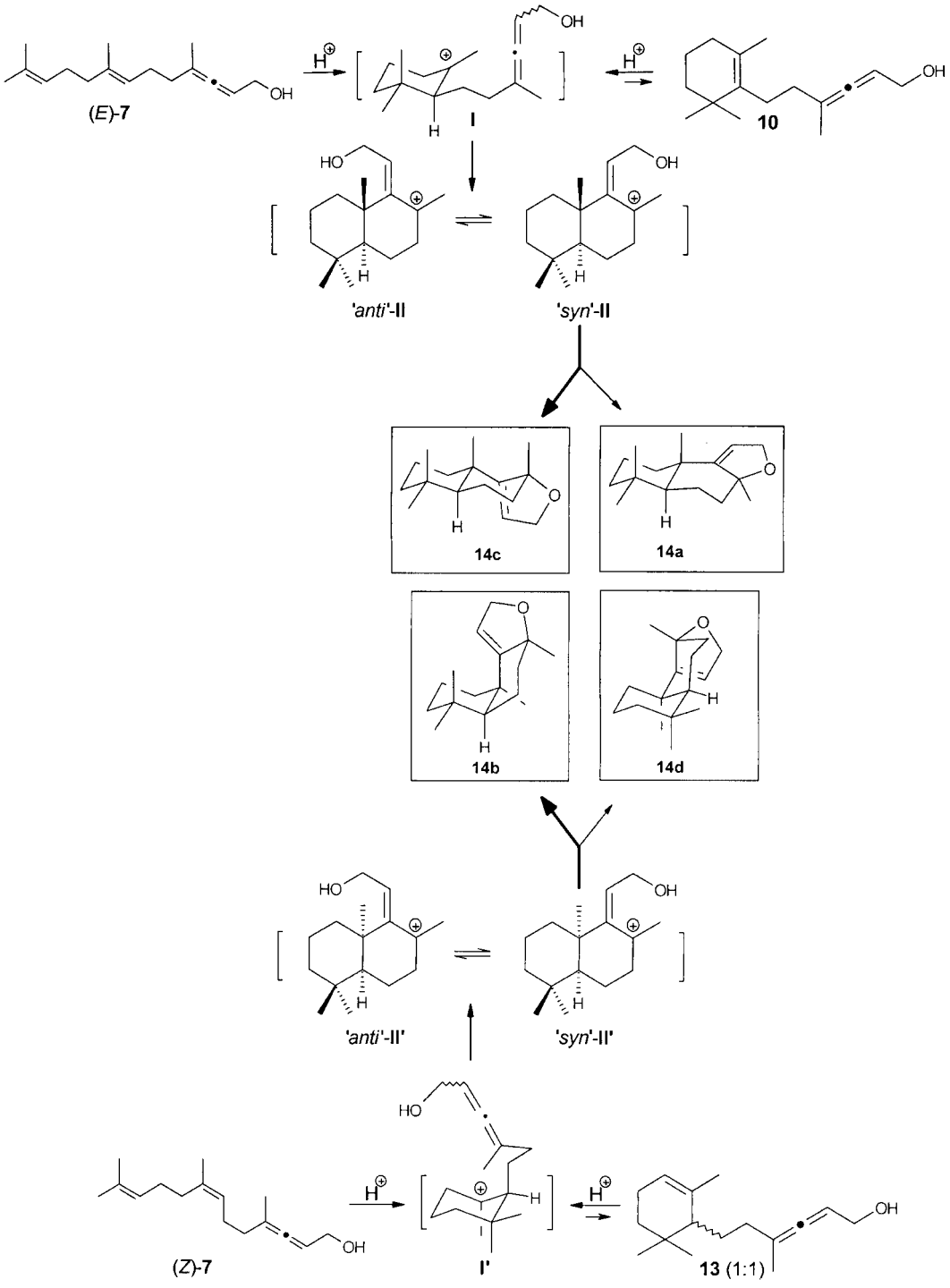
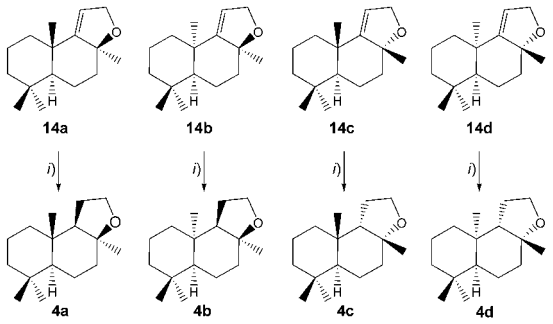


Table. *Acid-Mediated Cyclizations of* (E)*-and* (Z)-**7**, **10**, *and* **13**

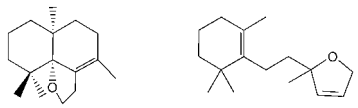
Entry	Substrate	Product distribution[a])[b])				Yield [%]
		14a	**14b**	**14c**	**14d**	
1[c])	(*E*)-**7**	2	10	88	< 0.5	68
2[c])	(*Z*)-**7**	< 0.5	83	11	6	84
3[c])	**10**	3	12	84	1	76
4[d])[e])	**10**	5	23	69	3	64
5	**13**	< 0.5	83	10	7	85

[a]) GC Analysis of distilled product after workup. [b]) Structural attributions by conversions of **14a**–**d** to **4a**–**d**:



i) H_2, [10% Pd/C], toluene, r.t.

[c]) Reaction conditions: substrate (1 g), FSO_3H (1 g), 2-nitropropane (10 ml), −90° to −30°. [d]) Reaction conditions: substrate (11 g), 95% aq. H_2SO_4 soln. (11 g), CH_2Cl_2, −40°. [e]) By-products:



15 (*ca.* 0.5%) **16** (*ca.* 2%)

selectivity), strongly points to the intermediacy of the diastereoisomeric cyclohexyl cations **I** and **I′**, respectively, both assumed to be 1:1 diastereoisomer mixtures. Thus, **I**, whose side chain is equatorial, can originate from (*E*)-**7** by cyclization of the chair-like, nascent cyclohexane A-ring, or from **10** *via* stereoselective axial protonation of the cyclohexenyl C=C bond[9]). Similarly, **I′**, whose side chain is axial, can be formed by cyclization of (*Z*)-**7** or by protonation of **13**, in which the side chain is pseudoaxial[10]). Cyclization of **I** to the allylic cation **II** ('*syn*'/'*anti*' diastereoisomer mixture) possessing a *trans* A/B ring junction proceeds *via* selective equatorial C–C bond formation, thus avoiding 1,3-diaxial nonbonding interactions with the axial Me–C(6′) group in ring A. Conversely, cyclization of **I′** to allylic cation **II′** ('*syn*'/'*anti*' mixture) with a *cis* A/B ring junction can only proceed *via* equatorial C–C bond formation. Our results clearly show

9) Kinetically controlled axial protonation of a cyclohexenyl C=C bond is stereoelectronically favored by hyperconjugative stabilization of the cyclohexyl cation by the developing C–H bond [1].

10) For evidence of this supposition, by molecular-mechanics calculations of a model system or by analogy with known work, see [1].

that interconversion of **I** and **I′**, by conformational inversion or *via* a rapid deprotonation/protonation process, is slower than subsequent cyclization[11]). It is also important to note that the high yields of isolated products, coupled with the fact that only '*syn*'-**II** and '*syn*'-**II′** can undergo ring closure to a dihydrofuran, mean that '*anti*'-**II** and '*anti*'-**II′** must be rapidly converted to their '*syn*' diastereoisomer under the reaction conditions[12]). Ring closure of the conformationally rigid '*syn*'-**II**, leading to either **14a** or **14c**, shows a strong preference for the latter diastereoisomer (selectivity $>20:1$). This stereoselectivity, attributed to a kinetic preference for equatorial C–O bond-formation opposite to the axial Me–C(9a) group, is reflected in the MM2 energies of **14a** and **14c**: 42.1 and 38.9 kcal/mol, respectively[13]). In contrast, the conformationally flexible '*syn*'-**II′**, able to afford either **14b** or **14d**, cyclizes in favor of the former diastereoisomer (selectivity $>10:1$), correlating again with their MM2 energies: 40.8 and 41.4 kcal/mol, respectively. Here however, the mechanistic interpretation is complicated by the fact that **I′** can cyclize to **II′** *via* two different transition states, in which the nascent B ring is in either a chair-like or a skew-boat conformation[14]). The former pathway differs from the latter in that the formation of **14b** necessitates conformational inversion of '*syn*'-**II′** prior to ring closure.

2.3. *Acid-Mediated Cyclization* (95% aq. H_2SO_4 solution/CH_2Cl_2) *of* **10**. To find more practical conditions for these acid-mediated cyclizations, we treated **10** with the same excess (2.3 mol-equiv.) of 95% aqueous H_2SO_4 solution in CH_2Cl_2 at $-40°$ during 3 h. Workup as before afforded a mixture of **14a** (5%), **14b** (23%), **14c** (69%), and **14d** (3%) in 64% yield (*Table*, *Entry 4*). Also isolated and characterized were the unsaturated tricyclic ether **15** (*ca.* 0.5% yield) and dihydrofuran **16** (*ca.* 2% yield). Although **14c** is the major product, this reaction is, thus, less selective than that with FSO_3H (*Table*, *Entry 3*). This is probably a consequence of the heterogeneous conditions, which may influence protonation/deprotonation processes by altering sensitive parameters such as effective acid concentration and thermal transfer. With regard to the by-products, whereas **16** is the anticipated product of protonation of the allenyl group followed by ring closure[15]), the formation of **15** is rationalized by cyclization of **10** to spirocyclic carbocation **III**, 1,2-alkyl shift to allylic carbocation **IV**, and final ring closure of the tetrahydrofuran ring (*Scheme 4*).

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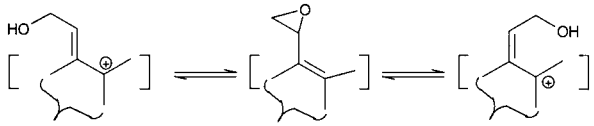
[11]) The formation of small amounts (10–15%) of **14b** and **14d** from (*E*)-**7** and **10**, and, conversely, of **14a** and **14c** from (*Z*)-**7** and **13**, resp., is assumed to be due to partial interconversion of **I** and **I′**.

[12]) Because of the high rotational barrier of an allyl cation (*ca.* 40 kcal/mol), this rapid '*anti*'-to-'*syn*' conversion must occur by external or internal quenching by a nucleophile followed by C–C bond rotation and regeneration of the allylic cation. The pathway involving an internal quench by the OH group is shown as follows:

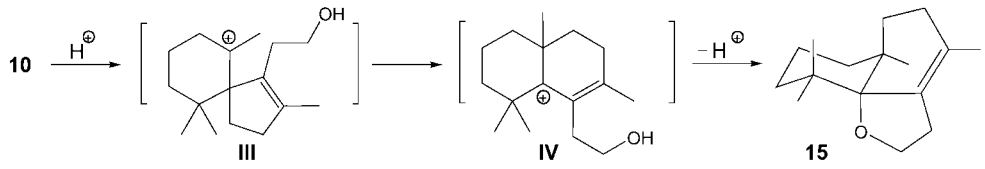


[13]) The MM2 energies were calculated with the MacroModel program [13].

[14]) Transition states involving skew-boat conformations have already been proposed in analogous cyclizations [1].

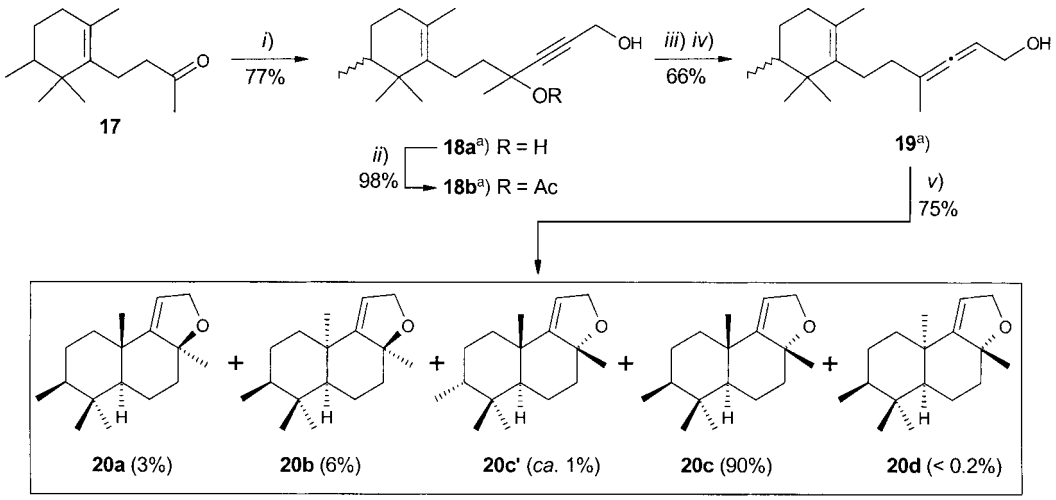
[15]) For the cyclization of allenic alcohols to dihydrofurans under acidic conditions, see [14].

Scheme 4



2.4. *Acid-Mediated Cyclization of Allenic Alcohol* **19** *to Tricyclic Ethers* **20a**–**d**. We now turned our attention to the cyclization of a higher homologue of **10**, possessing a supplementary Me–C(5′) group. We, thus, posed two questions. First, does this additional substitution affect the stereoselectivity of the cyclization reaction? Second, from a perfumery viewpoint, what are the organoleptic properties of tricyclic ethers resulting from this cyclization? Accordingly, by means of the same procedure as described above for the preparation of **10**, dihydro-β-irone (**17**) [2] was converted to **19** (1:1 diastereoisomer mixture) in four steps *via* intermediates **18a** and **18b** (1:1 diastereoisomer mixtures) in 50% overall yield (*Scheme 5*). Standard cyclization conditions (FSO_3H (2.3 mol-equiv.), 2-nitropropane, $-90°$ to $-30°$, 1 h) were now applied to **19**, to afford, after workup and distillation *in vacuo*, a mixture of **20a** (3%), **20b** (6%), **20c′** (*ca.* 1%), **20c** (90%), and **20d** (<0.2%) in 75% yield. The major component, **20c**, was readily isolated by crystallization, whereas column chromatography and prep. GC of the mother liquors allowed the isolation of a *ca.* 2:1 inseparable mixture **20b**/**20a**. Structures were assigned on the basis of GC/MS and NMR data, and corroborated by comparison with known dihydro analogs [2]. In contrast, due to

Scheme 5



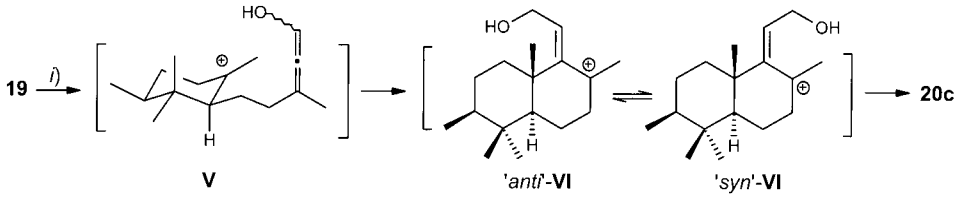
[a]) 1:1 mixture of diastereoisomers

i) Prop-2-yn-1-ol, KOH, THF, r.t. *ii*) Ac_2O, Et_3N, r.t. *iii*) Ethyl vinyl ether, cat. $TsOH \cdot H_2O$, toluene, $-20°$. *iv*) $LiAlH_4$, THF/toluene. *v*) FSO_3H, 2-nitropropane, $-90°$ to $-30°$.

ambiguous NMR spectral data, the structures attributed to **20c′** and **20d** are only speculative.

In close analogy to the cyclization of **10** (*vide supra*), the highly selective cyclization of **19** to **20c** can be rationalized by a nonsynchronous pathway involving stereoselective axial protonation of the cyclohexenyl C=C bond to carbocation **V** (1:1 diastereoisomer mixture), in which both the side chain at C(1′) and the Me–C(5′) group are equatorial, cyclization to allyl cation **VI** ('*syn*'/'*anti*' mixture), and final ring closure (*Scheme 6*).

Scheme 6



i) FSO_3H (2.3 mol-equiv.), 2-nitropropane, −90° to −30°; 75% yield.

2.5. *Organoleptic Properties of* **14c** *and* **20c**. Qualitative rather than quantitative odor evaluations were effected. Thus, in comparison with racemic *Ambrox*® (**4f**), olfactively very similar to (−)-**4f**, the benchmark ambergris odorant [15], **14c**, despite a lower substantivity, has a similar intensity, exhibiting the same characteristic amber, woody notes. Not unexpectedly, **20c**, its Me–C(7) homologue, is more substantive whilst retaining a typically strong amber, woody character.

3. Conclusions. – The key points of the foregoing work may be highlighted as follows: *i*) we have found a new type of *Brönsted* acid-mediated polyene cyclization in which the initiating group is an alkene and the terminating group is an allenic alcohol; *ii*) we have reinforced a mechanistic hypothesis postulating a nonsynchronous process, in which the stereochemical course of cyclization is directed by the conformation of an intermediate cyclohexyl cation; *iii*) we have developed an efficient synthetic access to novel, olfactively active, labdane tricyclic ethers of the *Ambrox*® family.

We thank Mr. *W. Thommen* and Mr. *R. Brauchli* for the measurements and interpretations of the NMR spectral data, Dr. *B. Winter* for the MM2 calculations, and Prof. *D. Arigoni* for helpful comments on mechanistic aspects.

Experimental Part

General. Commercially available reagents and solvents of adequate purity were used without further purification. Workup refers to washing of the org. layer to neutrality with aq. HCl soln. and/or $NaHCO_3$ and NaCl soln., drying (Na_2SO_4), filtration and evaporation of the solvent. Thin-layer chromatography (TLC): 0.25-mm pre-coated *60F*$_{254}$ silica-gel plates (*Merck*). Column chromatography (CC): silica gel (35–70 μm from *SDS*). Prep. GC: *JAS-2000* system equipped with *Supelco-SPB-1* capillary column (30 m, 0.53 mm i.d., with 5 μm film) at 185° (isotherm), He flow at 10 ml/min. Anal. GC: *Hewlett-Packard-5890* instrument; He as carrier gas; *Chrompack-DB-Wax* capillary column (15 m, 0.25 mm i.d.) t_R in min. Bulb-to-bulb distillation: *Büchi-GKR-50* oven; b.p. correspond to the air temp. IR Spectra (liquid film, unless otherwise stated): *Perkin-Elmer-297* spectrometer; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Bruker-DPX-400* or *-AV500* spectrometers; in $CDCl_3$; δ in ppm rel. to Me_4Si (=0 ppm), J in Hz; assignments by COSY45 and HMCQ experiments. MS: *Hewlett-*

Packard-5890 GC system equipped with a *DB-1* or *DB-WAX* capillary column (30 m, 0.25 mm i.d.) coupled with a *Hewlett-Packard MSD-5972* or *-5973* quadrupole mass spectrometer; electron energy *ca.* 70 eV; in *m/z* (rel. int. in % of the base peak).

*(7*E*)-4,8,12-Trimethyltrideca-7,11-dien-2-yne-1,4-diol* ((*E*)-**6a**). A mixture of (5*E*)-6,10-dimethylundeca-5,9-dien-2-one (*Aldrich*; (*E*)-**5**; 12 g, 0.062 mol) and prop-2-yn-1-ol (3.8 g, 0.068 mol) was added dropwise during 20 min to a stirred slurry of powdered KOH (26 g, 0.46 mol) in THF (90 ml) at 15° under N_2. After 3.5 h, the mixture was poured into a cold soln. of NH_4Cl (29 g) in H_2O (90 ml). The aq. layer was extracted (AcOEt), and the combined org. layer was washed with sat. aq. NaCl soln., dried (Na_2SO_4), and evaporated. CC (cyclohexane/AcOEt 7:3) and bulb-to-bulb distillation *i.v.* afforded (*E*)-**6a** (11.2 g, 72%). Viscous, colorless oil. B.p. 200–220°/0.04 mbar. IR: 3331 (br.), 2927, 1375, 1055, 600. ^{1}H-NMR (after exchange with D_2O): 1.49 (*s*, 3 H); 1.60 (*s*, 3 H); 1.64 (*s*, 3 H); 1.69 (*s*, 3 H); 1.70 (2 H); 1.90–2.30 (6 H); 4.29 (*s*, 2 H); 5.09 (br. *t*, *J* = 7, 1 H); 5.16 (*t*, *J* = 7, 1 H). ^{13}C-NMR: 136.0 (*s*); 131.5 (*s*); 124.3 (*d*); 123.7 (*d*); 89.4 (*s*); 81.8 (*s*); 68.3 (*s*); 50.8 (*t*); 43.4 (*t*); 39.7 (*t*); 29.6 (*q*); 26.7 (*t*); 25.7 (*q*); 23.5 (*t*); 17.7 (*q*); 16.1 (*q*). MS: 250 (< 0.5, M^+), 217 (2), 199 (2), 145 (12), 121 (20), 105 (34), 93 (30), 69 (94), 43 (100).

*(7*E*)-4-Hydroxy-4,8,12-trimethyltrideca-7,11-dien-2-ynyl Acetate* ((*E*)-**6b**). Et_3N (5.4 g, 0.054 mol) was added dropwise to a stirred mixture of (*E*)-**6a** (11.2 g, 0.045 mol) and Ac_2O (5.3 g, 0.052 mol) at 25° under N_2. After 15 min, the cooled mixture was poured into cold 10% aq. HCl soln. (55 ml) and extracted (Et_2O). The org. layer was washed successively with sat. aq. $NaHCO_3$ soln., H_2O, and sat. aq. NaCl soln., dried (Na_2SO_4), and evaporated. Bulb-to-bulb distillation afforded (*E*)-**6b** (12 g, 91%). Viscous, colorless oil. B.p. 120–140°/0.03 mbar. ^{1}H-NMR (after exchange with D_2O): 1.49 (*s*, 3 H); 1.59 (*s*, 3 H); 1.65 (*s*, 3 H); 1.69 (*s*, 3 H); 1.71 (2 H); 1.95–2.40 (6 H); 2.10 (*s*, 3 H); 4.71 (*s*, 2 H); 5.09 (br. *t*, *J* = 7, 1 H); 5.18 (*t*, *J* = 7, 1 H). MS: 292 (< 0.5, M^+), 217 (1), 199 (5), 145 (17), 121 (16), 105 (23), 93 (17), 69 (62), 43 (100).

*(7*E*)-4,8,12-Trimethyltrideca-2,3,7,11-tetraen-1-ol* ((*E*)-**7**). A soln. of ethyl vinyl ether (3.6 g, 0.049 mol) in toluene (5 ml) was added dropwise during 10 min to a stirred soln. of (*E*)-**6b** (12 g, 0.041 mol) in toluene (50 ml) containing $TsOH \cdot H_2O$ (60 mg) at −20° under N_2. After 10 min at −20°, TLC showed complete conversion of (*E*)-**6b** to a less polar product (R_f (cyclohexane/AcOEt 4:1) 0.40 compared to R_f 0.10 for (*E*)-**6b**), and this mixture was cooled to −50° prior to its dropwise addition during 5 min to a stirred slurry of $LiAlH_4$ (14 ml of a *ca.* 3.5M suspension in THF/toluene (*Fluka*); 0.049 mol) at 20° under N_2. After 2 h at 20°, H_2O (1.9 ml), 20% NaOH soln. (1.9 ml), and H_2O (9.5 ml) were added successively dropwise. Filtration (*Celite*) and evaporation of the filtrate afforded a pale-yellow oil (9.5 g), which was purified by CC (cyclohexane/AcOEt 4:1) to furnish, after distillation *i.v.* (*Vigreux* column), (*E*)-**7** (7.4 g, 77%). Colorless oil. B.p. 102°/0.03 mbar. R_f 0.25 (cyclohexane/AcOEt 4:1). IR: 3329 (br.), 2923, 1965, 1444, 1011. ^{1}H-NMR (after exchange with D_2O): 1.60 (*s*, 6 H); 1.68 (*s*, 3 H); 1.72 (*d*, *J* = 3, 3 H); 1.95–2.20 (8 H); 4.05 (*d*, *J* = 6, 2 H); 5.11 (2 H); 5.26 (*m*, 1 H). ^{13}C-NMR: 200.3 (*s*); 135.7 (*s*); 131.3 (*s*); 124.4 (*d*); 124.0 (*d*); 102.8 (*s*); 91.5 (*d*); 61.0 (*t*); 39.8 (*t*); 34.1 (*t*); 26.8 (*t*); 26.1 (*t*); 25.7 (*q*); 19.2 (*q*); 17.7 (*q*); 16.1 (*q*). MS: 234 (0.5, M^+), 173 (4), 145 (15), 131 (11), 119 (23), 105 (40), 91 (30), 69 (100), 41 (97).

*(7*Z*)-4,8,12-Trimethyltrideca-7,11-dien-2-yne-1,4-diol* ((*Z*)-**6a**). As described for (*E*)-**6a**, with *(7*Z*)-6,10-dimethylundeca-5,9-dien-2-one* (*Aldrich*; (*Z*)-**5**; 12 g, 0.062 mol): (*Z*)-**6a** (10.7 g, 69%). Viscous, colorless oil. B.p. (bulb-to-bulb dist.) 200–220°/0.05 mbar. R_f (cyclohexane/AcOEt 4:1) 0.08. IR: 3335 (br.), 2929, 1449, 1376, 1095, 1056, 999. ^{1}H-NMR (after exchange with D_2O): 1.48 (*s*, 3 H); 1.62 (*s*, 3 H); 1.69 (2 H); 1.70 (*s*, 6 H); 2.00–2.30 (6 H); 4.27 (*s*, 2 H); 5.13 (1 H); 5.16 (*t*, *J* = 7, 1 H). ^{13}C-NMR: 136.1 (*s*); 131.7 (*s*); 124.6 (*d*); 124.4 (*d*); 89.5 (*s*); 81.8 (*s*); 68.3 (*s*); 50.8 (*t*); 43.7 (*t*); 32.0 (*t*); 29.6 (2*q*); 26.6 (*t*); 25.7 (*q*); 23.4 (*t*); 17.7 (*q*). MS: 250 (< 0.5, M^+), 217 (2), 199 (82), 145 (15), 121 (18), 105 (29), 93 (32), 69 (100).

*(7*Z*)-4-Hydroxy-4,8,12-trimethyltrideca-7,11-dien-2-ynyl Acetate* ((*Z*)-**6b**). As described for (*E*)-**6b**, with (*Z*)-**6a** (11.4 g, 0.046 mol): (*Z*)-**6b** (12.5 g, 94%). Colorless oil. B.p. 127°/0.03 mbar. R_f (cyclohexane/AcOEt 4:1) 0.25. ^{1}H-NMR (after D_2O exchange): 1.48 (*s*, 3 H); 1.61 (*s*, 3 H); 1.68 (2 H); 1.69 (*s*, 3 H); 2.00–2.35 (6 H); 2.09 (*s*, 3 H); 4.70 (*s*, 2 H); 5.12 (*m*, 1 H); 5.17 (*t*, *J* = 7, 1 H). MS: 292 (< 0.5, M^+), 217 (3), 199 (7), 145 (17), 121 (18), 105 (26), 93 (23), 69 (89), 43 (100).

*(7*Z*)-4,8,12-Trimethyltrideca-2,3,7,11-tetraen-1-ol* ((*Z*)-**7**). As described for the preparation of (*E*)-**7**, with (*Z*)-**6b** (12.5 g, 0.043 mol): (*Z*)-**7** (6.5 g, 65%). Colorless oil. B.p. 99°/0.04 mbar. R_f (cyclohexane/AcOEt 4:1) 0.32. IR: 3329 (br.), 2926, 1965, 1445, 1376, 1012. ^{1}H-NMR (after exchange with D_2O): 1.61 (*s*, 3 H); 1.69 (2*s*, 6 H); 1.72 (*d*, *J* = 3, 3 H); 1.95–2.20 (8 H); 4.05 (*d*, *J* = 6, 2 H); 5.12 (2 H); 5.27 (*m*, 1 H). ^{13}C-NMR: 200.4 (*s*); 135.9 (*s*); 131.6 (*s*); 124.8 (*d*); 124.4 (*d*); 102.6 (*s*); 91.6 (*d*); 61.0 (*t*); 34.4 (*t*); 32.1 (*t*); 26.6 (*t*); 26.0 (*t*); 25.7 (*q*); 23.4 (*q*); 19.1 (*q*); 17.6 (*q*). MS: 234 (1, M^+), 173 (14), 145 (30), 131 (30), 119 (38), 105 (60), 91 (54), 69 (85), 41 (100).

4-Methyl-6-(2,6,6-trimethylcyclohex-1-en-1-yl)hex-2-yne-1,4-diol (**9a**). As described for (*E*)-**6a**, with 4-(2,6,6-trimethylcyclohex-1-en-1-yl)butan-2-one (**8**; 20 g, 0.103 mol): **9a** (19.1 g, 80%). Pale-yellow powder. Purification by recrystallization (petroleum ether). B.p. 80–100°. M.p. 83–84°. R_f (cyclohexane/AcOEt 1:1) 0.32. IR ($CHCl_3$): 3530, 3350 (br.), 2900, 2840, 1440, 1360, 1344, 1082, 1040, 980. ^{1}H-NMR (after exchange with D_2O): 1.00 (*s*, 6 H); 1.41 (*s*, 3 H); 1.50 (2 H); 1.57 (2 H); 1.61 (*s*, 3 H); 1.73 (2 H); 1.90 (br. *t*, *J* = 7, 2 H); 2.19 (2 H); 4.30 (*s*, 2 H). ^{13}C-NMR: 136.3 (*s*); 127.5 (*s*); 89.5 (*s*); 81.7 (*s*); 68.3 (*s*); 50.7 (*t*); 43.5 (*t*); 39.9 (*t*); 35.2 (*s*); 32.8 (*t*); 29.3 (*q*); 23.6 (*t*); 19.8 (*q*); 19.6 (*t*). MS: 250 (< 0.5, M^+), 232 (9), 217 (19), 161 (37), 145 (40), 133 (40), 121 (100), 105 (79), 95 (87), 81 (80).

4-Hydroxy-4-methyl-6-(2,6,6-trimethylcyclohex-1-en-1-yl)hex-2-ynyl Acetate (**9b**). As described for (*E*)-**6b**, with **9a** (25 g, 0.1 mol): **9b** (28.3 g, 97%). Viscous, colorless oil. B.p. 144–150°/0.05 mbar. R_f (cyclohexane/AcOEt 7:3) 0.41. IR ($CHCl_3$): 3540, 3380 (br.), 2900, 2850, 1722, 1440, 1368, 1350, 1220, 1100, 958. ^{1}H-NMR (after exchange with D_2O): 1.00 (*s*, 6 H); 1.41 (2 H); 1.49 (*s*, 3 H); 1.56 (2 H); 1.60 (*s*, 3 H); 1.73 (2 H); 1.90 (br. *t*, *J* = 7, 2 H); 2.09 (*s*, 3 H); 2.19 (2 H); 4.71 (*s*, 2 H). MS: 292 (< 0.5, M^+), 274 (8), 217 (31), 199 (27), 161 (36), 143 (44), 121 (100), 105 (71), 95 (94), 81 (76).

4-Methyl-6-(2,6,6-trimethylcyclohex-1-en-1-yl)hexa-2,3-dien-1-ol (**10**). As described for (*E*)-**7**, with **9b** (22.5 g, 0.077 mol): **10** (15 g, 83%). Colorless oil. B.p. (bulb-to-bulb dist.) 150–180°/0.05 mbar. R_f (cyclohexane/AcOEt 7:3) 0.41. IR ($CHCl_3$ soln.): 3560, 3400 (br.), 2920, 2850, 1944, 1460, 1370, 1358, 1108, 1072, 990. ^{1}H-NMR (after exchange with D_2O): 0.98 (*s*, 6 H); 1.41 (2 H); 1.56 (2 H); 1.58 (*s*, 3 H); 1.74 (*d*, *J* = 3, 3 H); 1.90 (br. *t*, *J* = 7, 2 H); 1.99 (2 H); 2.08 (2 H); 4.08 (*d*, *J* = 5, 2 H); 5.30 (*m*, 1 H). ^{13}C-NMR: 200.0 (*s*); 137.0 (*s*); 127.4 (*s*); 103.6 (*s*); 91.6 (*d*); 61.1 (*t*); 39.9 (*t*); 35.0 (*s*); 34.4 (*t*); 32.8 (*t*); 28.6 (2*q*); 27.1 (*t*); 19.8 (*q*); 19.6 (*t*), 19.2 (*q*). MS: 234 (2, M^+), 219 (5), 145 (36), 133 (29), 121 (39), 107 (46), 95 (100), 81 (70).

4-Methyl-6-(2,6,6-trimethylcyclohex-2-en-1-yl)hex-2-yn-1,4-diol (**12a**; 1:1 diastereoisomer mixture). As described for (*E*)-**6a**, with *4-(2,6,6-trimethylcyclohex-2-enyl)butan-2-one* (**11**; 20 g, 0.103 mol): **12a** (20.5 g, 86%). Viscous, colorless oil. Purification by CC (cyclohexane/AcOEt 7:3) and bulb-to-bulb distillation *i.v.* B.p. 200–220°/0.5 mbar. R_f (cyclohexane/AcOEt 4:1) 0.13. IR: 3332 (br.), 2951, 1364, 1143, 1057, 1001. ^{1}H-NMR (after exchange with D_2O): 0.87 (*s*, 3 H); 0.94 (*s*, 3 H); 1.13 (*m*, 1 H); 1.46 (*s*, 3 H); 1.35–1.80 (6 H); 1.68 (*s*, 3 H); 1.96 (2 H); 4.26 (*s*, 2 H); 5.31 (1 H). ^{13}C-NMR: 136.2 (*s*); 120.5 (*d*); 89.6 (*s*); 81.6 (*s*); 68.4 (*s*); 50.7 (*t*); 49.2 (*d*); 43.6 (*t*); 32.7 (*s*); 31.8 (*t*); 29.4 (*q*); 27.7 (*q*); 27.6 (*q*); 25.6 (*t*); 23.4 (*q*); 23.0 (*t*). MS: 250 (0.5, M^+), 136 (100), 121 (87), 105 (53), 95 (59), 81 (98), 43 (85).

4-Hydroxy-4-methyl-6-(2,6,6-trimethylcyclohex-2-en-1-yl)hex-2-ynyl Acetate (**12b**; 1:1 diastereoisomer mixture). As described for (*E*)-**6b**, with **12a** (21.5 g, 0.086 mol): **12b** (23.2 g, 92%). Viscous, colorless oil. B.p. 135°/0.05 mbar. R_f (cyclohexane/AcOEt 4:1) 0.29. ^{1}H-NMR (after exchange with D_2O): 0.88 (*s*, 3 H); 0.94 (*s*, 3 H); 1.13 (*m*, 1 H); 1.35–1.80 (6 H); 1.47 (*s*, 3 H); 1.68 (*s*, 3 H); 1.96 (2 H); 2.09 (*s*, 3 H); 4.69 (*s*, 2 H); 5.32 (1 H). ^{13}C-NMR: 170.3 (*s*); 136.2 (*s*); 120.5, 120.4 (2 *d*); 90.6 (*s*); 77.2 (*s*); 68.3 (*s*); 52.3 (*t*); 49.1 (*d*); 43.6 (*t*); 32.7 (*s*); 31.8 (*t*); 29.4 (*q*); 27.7 (*q*); 27.5 (*q*); 25.6, 25.5 (2 *t*); 23.3 (*q*); 23.0 (*t*); 20.7 (*q*). MS: 292 (< 0.5, M^+), 158 (13), 143 (18), 136 (96), 121 (60), 81 (43), 43 (100).

4-Methyl-6-(2,6,6-trimethylcyclohex-2-en-1-yl)hexa-2,3-dien-1-ol (**13**; 1:1 diastereoisomer mixture). As described for (*E*)-**7**, with **12b** (22.5 g, 0.077 mol): **13** (14.3 g, 79%). Colorless oil. B.p. 95–100°/0.03 mbar. R_f (cyclohexane/AcOEt 4:1) 0.27. IR: 3322 (br.), 2933, 1965, 1446, 1384, 1013. ^{1}H-NMR (after exchange with D_2O): 0.87 (*s*, 3 H); 0.92 (*s*, 3 H); 1.12 (*m*, 1 H); 1.35–1.75 (4 H); 1.67 (*s*, 3 H); 1.72 (*d*, *J* = 3, 3 H); 1.85–2.10 (4 H); 4.07 (*d*, *J* = 7, 2 H); 5.27 (*m*, 1 H); 5.31 (*m*, 1 H). ^{13}C-NMR: 200.3 (*s*); 136.4 (*s*); 120.3 (*d*); 103.2 (*s*); 91.4 (*d*); 61.1 (*t*); 49.1, 49.0 (2 *d*); 34.4 (*t*); 32.6 (*s*); 31.7 (*t*); 29.1 (*t*); 27.6, 27.5 (2 *q*). MS: 234 (1, M^+), 201 (11), 145 (18), 136 (36), 121 (100), 107 (47), 93 (60), 81 (73).

Acid-Mediated Cyclization (FSO_3H/2-nitropropane) *of* (E)-**7**, (Z)-**7**, **10**, *and* **13**. *(3a*RS,*5a*RS,*9a*RS)-, (3a*RS,*5a*RS,*9a*SR)-, (3a*RS,*5a*SR,*9a*SR)-, and (3a*RS,*5a*SR,*9a*RS)-2,3a,4,5,5a,6,7,8,9,9a-Decahydro-3a,6,6,9a-tetramethylnaphtho[2,1-*b*]furan* (**14a–d**). A soln. of the substrate (1 g, 4.3 mmol) in 2-nitropropane (10 ml) was added dropwise during 10 min to a stirred slurry of FSO_3H (*Bayer*; 1 g, 10 mmol) in 2-nitropropane (10 ml) at −90° (cooling bath: liq. N_2/MeOH) under N_2. After 15 min at −90°, the dark-violet mixture was allowed to attain −30° during 30 min and then poured into a cold soln. of $NaHCO_3$ (6 g) in H_2O (50 ml). Extraction (Et_2O), workup, and bulb-to-bulb distillation *i.v.* (b.p. 140–160°/0.04 mbar) afforded the mixture **14a–d** as a pale-yellow oil (*ca.* 0.7–0.9 g) whose composition was determined by GC (column temp. 100–220°, 15°/min; see *Table*): t_R 5.63 (**14a**), 5.69 (**14b**), 6.17 (**14c**), and 6.40 (**14d**). A combination of prep. GC and CC (toluene) was used to isolate pure samples of each diastereoisomer for spectral characterization.

Data of **14a**: ^{1}H-NMR: 0.88 (*s*, 3 H); 0.91 (*s*, 3 H); 1.13 (*s*, 3 H); 1.38 (*s*, 3 H); 1.00–2.20 (11 H); 4.37 (*dd*, *J* = 13, 3, 1 H); 4.58 (*dd*, *J* = 13, 1.5, 1 H); 5.45 (br. *s*, 1 H). ^{13}C-NMR: 159.4 (*s*, C(9b)); 116.6 (*d*, C(1)); 86.4 (*s*, C(3a)); 71.8 (*t*, C(2)); 45.2 (*d*, C(5a)); 42.3 (*t*, C(4)); 40.3 (*t*, C(7)); 37.6 (*s*, C(9a)); 33.5 (*q*, Me_α–C(6)); 33.4 (*s*,

C(6)); 33.3 (*t*, C(9)); 26.7 (*q*, *Me*-C(3a)); 26.0 (*q*, *Me*-C(9a)); 21.4 (*q*, Me_β–C(6)); 19.4 (*t*, C(8)); 17.7 (*t*, C(5)). MS: 234 (12, M^+), 219 (100), 149 (17), 123 (17), 110 (31), 97 (69), 81 (49), 69 (32).

Data of **14b**: ^{1}H-NMR: 0.93 (*s*, 3 H); 0.94 (*s*, 3 H); 1.15 (*s*, 3 H); 1.42 (*s*, 3 H); 1.00–2.00 (11 H); 4.47 (*dd*, *J* = 13, 3, 1 H); 4.56 (*dd*, *J* = 13, 1.5, 1 H); 5.42 (br. *s*, 1 H). ^{13}C-NMR: 150.8 (*s*, C(9b)); 116.6 (*d*, C(1)); 86.6 (*s*, C(3a)); 71.5 (*t*, C(2)); 50.5 (*d*, C(5a)); 44.2 (*t*, C(7)); 39.9 (*t*, C(9)); 37.2 (*s*, C(9a)); 37.0 (*t*, C(4)); 34.8 (*s*, C(6)), 33.1 (*q*, Me_α–C(6)); 32.1 (*q*, *Me*–C(9a)); 28.0 (*q*, *Me*–C(3a); 26.1 (*q*, Me_β–C(6)); 20.3 (*t*, C(5)); 19.0 (*t*, C(8)). MS: 234 (7, M^+), 219 (65), 110 (70), 97 (100), 81 (58), 69 (30).

Data of **14c**: M.p. 37–40°. IR ($CHCl_3$): 2950, 1460, 1380, 1140, 1100, 1060, 1020. ^{1}H-NMR: 0.86 (*s*, 3 H); 0.87 (*s*, 3 H); 0.94 (*dd*, *J* = 13, 3.5, 1 H); 1.08 (*s*, 3 H); 1.16 (*m*, 1 H); 1.38 (*s*, 3 H); 1.35–1.80 (8 H); 2.00 (*dt*, *J* = 13, 3.5, 1 H); 4.47 (*dd*, *J* = 13, 3.5, 1 H); 4.58 (*dd*, *J* = 13, 1.5, 1 H); 5.23 (br. *s*, 1 H). ^{13}C-NMR: 156.5 (*s*, C(9b)); 113.1 (*d*, C(1)); 87.2 (*s*, C(3a)); 72.1 (*t*, C(2)); 55.3 (*d*, C(5a)); 42.2 (*t*, C(4)); 42.1 (*t*, C(7)); 38.1 (*t*, C(9)); 37.7 (*s*, C(9a)); 33.6 (*s*, C(6)); 33.4 (*q*, Me_α–C(6)); 26.4 (*q*, *Me*–C(3a)); 21.5 (*q*, Me_β–C(6)); 20.3 (*t*, C(5)); 19.9 (*q*, *Me*–C(9a)); 18.6 (*t*, C(8)). MS: 234 (19, M^+), 219 (100), 191 (32), 110 (36), 97 (66), 81 (51), 69 (37).

Data of **14d**: ^{1}H-NMR: 0.91 (*s*, 3 H); 1.17 (*s*, 3 H); 1.39 (*s*, 3 H); 1.41 (*s*, 3 H); 1.00–2.00 (11 H); 4.47 (*dd*, *J* = 13, 3, 1 H); 4.59 (*dd*, *J* = 13, 1.5, 1 H); 5.47 (br. *s*, 1 H). ^{13}C-NMR: 154.8 (*s*, C(9b)); 118.5 (*d*, C(1)); 86.6 (*s*, C(3a)); 71.6 (*t*, C(2)); 52.5 (*d*, C(5a)); 40.5 (*t*, C(4)); 39.6 (*s*, C(9a)); 34.9 (*t*, C(7)); 33.7 (*s*, C(6)); 33.7 (*q*, Me_β–C(6)); 32.2 (*t*, C(9)); 31.4 (*q*, Me_α–C(6)); 27.6 (*q*, *Me*–C(9a)); 25.7 (*q*, *Me*–C(3a)); 23.9 (*t*, C(5)); 19.3 (*t*, C(8)). MS: 234 (8, M^+), 219 (40), 149 (11), 110 (58), 97 (100), 81 (32).

Catalytic Hydrogenation of **14a–d**: *(3a*RS,*5a*RS,*9a*RS,*9b*SR*)-, (3a*RS,*5a*RS,*9a*SR,*9b*SR*)-, (3a*RS,*5a*SR,-*9a*SR,*9b*SR*)-, and (3a*RS,*5a*SR,*9a*RS,*9b*SR*)-Dodecahydro-3a,6,6,9a-tetramethylnaphtho[2,1*-b*]furan* (**4a–d**). A stirred soln. of **14a** (8%), **14b** (24%), **14c** (64%), and **14d** (4%) (0.1 g, 0.43 mmol) in toluene (2 ml) containing 10% Pd/C (0.1 g) was hydrogenated (1 bar H_2) at r.t. during 3 h. After filtration (*Celite*), the product was analyzed by GC and, by comparison with authentic samples of **4a–d** [5], shown to consist of a mixture of **4a** (8%), **4b** (4%), **4c** (63%), and **4d** (4%), besides unreacted **14b** (20%) and **14c** (1%). GC (column temp. 100–220°, 15°/min): t_R 5.91 (**4a**), 6.06 (**4b**), 6.27 (**4c**), and 6.37 (**4d**).

Acid-Mediated Cyclization (95% aq. H_2SO_4 soln./CH_2Cl_2) *of* **10**. A soln. of **10** (11 g, 0.044 mol) in CH_2Cl_2 (30 ml) was added dropwise during 1 h to a mechanically stirred slurry of 95% aq. H_2SO_4 soln. (11 g, 0.11 mol) in CH_2Cl_2 (110 ml) at −40° under N_2. The dark-red mixture was stirred for a further 3 h at −40° and then poured slowly into a cold soln. of $NaHCO_3$ (20 g) in H_2O (250 ml), which was stirred during 30 min, allowing the mixture to attain r.t. The resulting white emulsion was partially concentrated *i.v.* (30°/15 mbar), and the residue was extracted with Et_2O. Workup gave a viscous orange oil (11.2 g), which was distilled *i.v.* (*Vigreux* column): colorless oil (6.5 g, 64%) composed of **14a** (5%), **14b** (23%), **14c** (69%), and **14d** (3%). Trace amounts of *(6a*RS,*10a*SR*)-3,5,6,6a,7,8,9,10-octahydro-4,6a,10,10-tetramethyl-2*H*-naphtho[8a,1-*b*]furan* (**15**; *ca.* 0.5% of crude product mixture) and *2,5-dihydro-2-methyl-2-[2-(2,6,6-trimethylcyclohex-1-en-1-yl)ethyl]furan* (**16**; *ca.* 2.5% of crude product mixture) were isolated from head fractions and purified by CC (toluene) and bulb-to-bulb distillation *i.v.* (b.p. 130–150°/0.05 mbar).

Data of **15**: R_f (toluene) 0.36. IR ($CHCl_3$): 2930, 1458, 1380, 1362, 1040, 1020, 970. ^{1}H-NMR: 0.71 (*s*, 3 H); 0.85 (*s*, 3 H); 0.92 (*s*, 3 H); 1.10 (*m*, 2 H); 1.27 (br. *d*, *J* = 11, 1 H); 1.39 (*m*, 1 H); 1.55–1.70 (3 H); 1.70 (*s*, 3 H); 1.90–2.20 (3 H); 2.52 (2 H); 3.60 (*dd*, *J* = 18, 9, 1 H); 4.02 (*ddd*, *J* = 18, 7.5, 3.5, 1 H). ^{13}C-NMR: 131.8 (*s*, C(3a)); 126.3 (*s*, C(4)); 87.6 (*s*, C(10a)); 67.0 (*t*, C(2)); 40.4 (*s*, C(10)); 38.1 (*s*, C(6a)); 37.1 (*t*, C(9)); 36.7 (*t*, C(7)); 31.5 (*t*, C(3)); 30.5 (*q*, Me_α–C(10)); 29.8 (*t*, C(6)); 28.3 (*t*, C(5)); 26.6 (*q*, *Me*–C(6a)); 24.5 (*q*, Me_β–C(10)); 20.3 (*q*, *Me*–C(4)); 18.3 (*t*, C(8)). MS: 234 (4, M^+), 219 (2), 150 (100), 135 (28), 91 (11), 79 (9).

Data of **16**: R_f (toluene) 0.30. IR ($CHCl_3$): 2950, 1460, 1082, 1048, 916. ^{1}H-NMR: 0.97 (*s*, 3 H); 0.98 (*s*, 3 H); 1.29 (*s*, 3 H); 1.40 (2 H); 1.58 (*s*, 3 H); 1.50–1.75 (4 H); 1.89 (*t*, *J* = 7, 2 H); 2.00 (*m*, 2 H); 4.65 (*m*, 2 H); 5.71 (*dt*, *J* = 7, 3, 1 H); 5.83 (br. *d*, *J* = 7, 1 H). ^{13}C-NMR: 137.2 (*s*); 133.6 (*d*); 126.8 (*s*); 125.6 (*d*); 90.4 (*s*); 74.8 (*t*); 41.2 (*t*); 40.0 (*t*); 35.1 (*s*); 32.8 (*t*); 28.7 (2*q*); 26.3 (*q*); 23.2 (*t*); 19.7 (*q*); 19.6 (*t*). MS: 234 (1, M^+), 121 (5), 95 (19), 83 (100), 55 (10).

4-Methyl-6-(2,5,6,6-tetramethylcyclohex-1-en-1-yl)hex-2-yne-1,4-diol (**18a**; 1:1 diastereoisomer mixture). A mixture of *4-(2,5,6,6-tetramethylcyclohex-1-en-1-yl)butan-2-one* [2] (**17**; 13 g, 0.061 mol; R_f (cyclohexane/AcOEt 7:3) 0.55) and prop-2-yn-1-ol (4 g, 0.071 mol) was added dropwise during 1.5 h to a mechanically stirred slurry of powdered KOH (26 g, 0.46 mol) in THF (100 ml) at 20° under N_2. After 3 h at 20°, the brown mixture was poured into a cold soln. of NH_4Cl (28 g) in H_2O (100 ml). Extraction (Et_2O), workup, CC (cyclohexane/AcOEt 7:3), and bulb-to-bulb distillation *i.v.* afforded **18a** (12.3 g, 77%). Viscous, pale-yellow oil. B.p. 180–200°/0.5 mbar. R_f (cyclohexane/AcOEt 7:3) 0.14. IR ($CHCl_3$): 3620, 3388 (br.), 3019, 2970, 1374, 1215, 1056, 932. ^{1}H-NMR (after exchange with D_2O): 0.85 (*s*, 3 H); 0.87 (*d*, *J* = 7, 3 H); 1.02 (2*s*, 3 H); 1.25–2.05 (7 H); 1.50 (*s*, 3 H); 1.62 (*s*, 3 H); 2.20 (*m*, 2 H); 4.30 (*s*, 2 H). ^{13}C-NMR: 136.4 (*s*); 127.2 (*s*); 89.5 (*s*); 81.7 (*s*); 68.3 (*s*); 50.7

(*t*); 43.5 (*t*); 39.4 (*d*); 38.4 (*s*); 31.7 (*t*); 29.3 (*q*); 27.3 (*t*); 27.1 (*q*); 23.9 (*t*); 21.8 (*q*); 19.9 (*q*); 16.7 (*q*). MS: 264 (< 0.5, M^+), 246 (3), 231 (11), 145 (34), 135 (82), 121 (57), 107 (66), 95 (78), 43 (100).

4-Hydroxy-4-methyl-6-(2,5,6,6-tetramethylcyclohex-1-en-1-yl)hex-2-ynyl Acetate (**18b**; 1:1 diastereoisomer mixture). As described for (*E*)-**6b**, with **18a** (6 g, 0.022 mol): **18b** (6.8 g, 98%). Viscous, pale-yellow oil. B.p. 145–148°/0.05 mbar. R_f (cyclohexane/AcOEt 7:3) 0.38. IR ($CHCl_3$): 3599, 3480 (br.), 3019, 2970, 1737, 1434, 1377, 1216, 1027, 965. ^{1}H-NMR (after exchange with D_2O): 0.85 (*s*, 3 H); 0.88 (*d*, *J* = 7, 3 H); 1.02 (*s*, 3 H); 1.25–2.30 (9 H); 1.50 (*s*, 3 H); 1.62 (*s*, 3 H); 2.10 (*s*, 3 H); 4.72 (*s*, 2 H). ^{13}C-NMR: 170.3 (*s*); 136.3 (*s*), 127.2 (*s*); 90.6 (*s*); 77.3 (*s*); 68.2 (*s*); 52.3 (*t*); 43.5 (*t*); 39.4 (*d*); 38.4 (*s*); 31.7 (*t*); 29.3 (*q*); 27.3 (*t*); 27.0 (*q*); 23.9 (*t*); 21.8 (*q*); 20.7 (*q*); 19.9 (*q*); 16.6 (*q*). MS: 306 (0, M^+), 288 (1), 231 (8), 213 (9), 175 (20), 157 (20), 145 (23), 135 (58), 121 (52), 107 (40), 95 (45), 43 (100).

4-Methyl-6-(2,5,6,6-tetramethylcyclohex-1-en-1-yl)hexa-2,3-dien-1-ol (**19**; 1:1 diastereoisomer mixture). As described for (*E*)-**7**, with **18b** (6.4 g, 0.021 mol): **19** (3.4 g, 66%). Viscous, colorless oil. B.p. 108–114°/0.05 mbar. R_f (toluene/AcOEt 9:1) 0.32. IR ($CHCl_3$): 3612, 3480, (br.), 3018, 2970, 1373, 1215, 1008. ^{1}H-NMR (after exchange with D_2O): 0.83 (*s*, 3 H); 0.88 (*d*, *J* = 7, 3 H); 1.00 (*s*, 3 H); 1.25–1.60 (3 H); 1.59 (*s*, 3 H); 1.75 (*d*, *J* = 3, 3 H); 1.65–2.20 (6 H); 4.09 (*d*, *J* = 7, 2 H); 5.31 (*m*, 1 H). ^{13}C-NMR: 200.0 (*s*); 137.1 (*s*); 127.1 (*s*); 103.5 (*s*); 91.6 (*d*); 61.2 (*t*); 39.4 (*d*); 38.2 (*d*); 34.5 (*t*); 31.7 (*t*); 27.3 (*t*); 27.0 (*q*); 21.8 (*q*); 19.9 (*q*); 19.2 (*q*); 16.7 (*q*). MS: 248 (< 0.5, M^+), 147 (30), 133 (39), 121 (55), 109 (57), 95 (100), 81 (48), 67 (57).

*(3a*RS,*5a*RS,*7*RS,*9a*RS*)-, (3a*RS,*5a*RS,*7*RS,*9a*SR*)-, (3a*RS,*5a*SR,*7*RS,*9a*SR*)-, (3a*RS,*5a*SR,*7*SR,*9a*SR*)-, and (3a*RS,*5a*SR,*7*SR,*9a*RS*)-2,3a,4,5,5a,6,7,8,9,9a-Decahydro-3a,6,6,7,9a-pentamethylnaphtho[2,1-*b*]furan* (**20a**, **20b**, **20c′**, **20c**, and **20d**, resp.). A soln. of **19** (1.6 g, 6.3 mmol) in 2-nitropropane (8 ml) was added dropwise during 15 min to a stirred slurry of FSO_3H (1 ml, 0.017 mmol) in 2-nitropropane (10 ml) at −90° under N_2. After 15 min at −90°, the dark-violet mixture was allowed to attain −30° during 1 h and then poured into a cold soln. of $NaHCO_3$ (6 g) in H_2O (50 ml). Extraction (Et_2O), workup, and bulb-to-bulb distillation *i.v.* (b.p. 140–160°/0.04 mbar) afforded the crude mixture **20a**–**d**, which was analyzed by GC: in ascending order of elution, **20a** (3%), **20b** (6%), **20c′** (*ca.* 1%), **20c** (90%), and **20d** (< 0.2%). Repeated low-temperature recrystallization (petroleum ether) afforded **20c** (0.79 g, 50%). White crystals. M.p. 86–88°. R_f (toluene/cyclohexane, 19:1) 0.32.

Data of **20c**: IR ($CHCl_3$): 2971, 1456, 1378, 1215, 1136, 1056, 1014, 855. ^{1}H-NMR: 0.70 (*s*, 3 H); 0.85 (*d*, *J* = 7, 3 H); 0.89 (*s*, 3 H); 0.92 (*m*, 1 H); 1.06 (*s*, 3 H); 1.20 (*m*, 1 H); 1.30–1.60 (5 H); 1.39 (*s*, 3 H); 1.68–1.78 (2 H); 2.00 (*m*, 1 H); 4.47 (*dd*, *J* = 11.5, 3, 1 H); 4.58 (*d*, *J* = 11.5, 1 H); 5.23 (br. *s*, 1 H). ^{13}C-NMR: 156.6 (*s*, C(9b)); 113.3 (*d*, C(1)); 86.9 (*s*, C(3a)); 72.1 (*t*, C(2)); 56.1 (*d*, C(5a)); 42.6 (*d*, C(7)); 42.0 (*t*, C(4)); 37.9 (*t*, C(9)); 36.7 (*s*, C(6)); 29.3 (*q*, Me_α–C(6)); 27.4 (*t*, C(8)); 26.3 (*q*, *Me*–C(3a)); 20.4 (*t*, C(5)); 19.8 (*q*, C(9a)); 16.4 (*q*, *Me*–C(7)); 16.3 (*q*, Me_β–C(6)). MS: 248 (12, M^+), 233 (58), 163 (11), 149 (43), 97 (100).

CC (toluene/AcOEt 19:1) and prep. GC of the mother liquors from the recrystallization (*vida supra*) resulted in the isolation of two fractions. *Fraction 1* (colorless oil; 80 mg, 5%) is a *ca.* 2:1 inseparable mixture **20b**/**20a**. B.p. 140–160°/0.04 mbar. R_f (toluene/AcOEt 19:1) 0.36. IR ($CHCl_3$): 2970, 1457, 1378, 1215, 1053.

Data of **20a**: ^{1}H-NMR: 0.75 (*s*, 3 H); 0.85 (*d*, *J* = 7, 3 H); 0.88 (*s*, 3 H); 1.10 (*s*, 3 H); 1.37 (*s*, 3 H); 4.38 (*dd*, *J* = 12, 3, 1 H); 4.46 (*dd*, *J* = 12, 3, 1 H); 5.44 (br. *s*, 1 H). ^{13}C-NMR: 159.3 (*s*, C(9b)); 116.6 (*d*, C(1)); 86.4 (*s*, C(3a)); 71.9 (*t*, C(2)); 48.5 (*d*, C(5a)); 40.3 (*t*, C(4)); 39.5 (*d*, C(7)); 37.1 (*s*, C(9a)); 36.5 (*s*, C(6)); 33.9 (*t*, C(9)); 31.4 (*q*, Me_α–C(6)); 29.4 (*q*, Me_β–C(6)); 28.2 (*t*, C(8)); 25.7 (*q*, *Me*–C(3a)); 17.9 (*t*, C(5)); 16.4 (*q*, *Me*–C(7)); 15.4 (*q*, *Me*–C(9a)). MS: 248 (8, M^+), 233 (50), 149 (39), 123 (20), 110 (19), 97 (100), 81 (32).

Data of **20b**: ^{1}H-NMR: 0.87 (*d*, *J* = 7, 3 H); 0.93 (*s*, 3 H); 0.98 (*s*, 3 H); 1.24 (*s*, 3 H); 1.40 (*s*, 3 H); 4.50 (br. *d*, *J* = 12, 1 H); 4.58 (br. *d*, *J* = 12, 1 H); 5.42 (br. *s*, 1 H). ^{13}C-NMR: 154.6 (*s*, C(9b)); 116.2 (*d*, C(1)); 86.9 (*s*, C(3a)); 72.0 (*t*, C(2)); 46.5 (*s*, C(5a)); 43.0 (*d*, C(7)); 38.8 (*t*, C(4)); 37.8 (*s*, C(9a)); 36.4 (*s*, C(6)); 34.3 (*t*, C(9)); 29.9 (*q*, Me_α–C(6)); 29.0 (*q*, Me_β–C(6)); 27.6 (*q*, *Me*–C(3a)); 26.8 (*q*, *Me*–C(9a)); 26.6 (*t*, C(8)); 21.1 (*t*, C(5)); 16.2 (*q*, Me–C(7)). MS: 248 (4, M^+), 233 (18), 149 (11); 110 (97), 97 (100), 81 (30).

Fraction 2 (colorless oil; 40 mg, 2.5%) is a *ca.* 4:15:1 mixture **20c′**/**20c**/**20d**. B.p. 140–160°/0.04 mbar. R_f (toluene/AcOEt 19:1) 0.32–0.36.

Data of **20c′**: MS: 248 (12, M^+), 233 (75), 191 (32), 149 (55), 110 (56), 97 (100), 81 (48).

Data of **20d**: MS: 248 (4, M^+), 233 (21), 149 (25), 110 (97), 97 (100), 81 (26).

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