A New Approach to Sesquiterpene Arenes of the 9,11-Drimenyl Type (= [(1*E*,2*RS*,4a*RS*,8a*RS*)-Octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H*)-ylidene] methyl Type)

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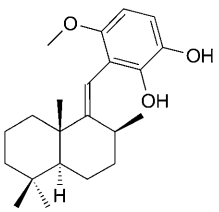
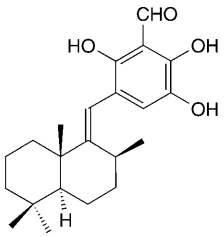
A new reaction sequence for the synthesis of the sesquiterpene arenes (±)-wiedendiol B ((±)-**1**) and the siphonodictyal B derivative (±)- **21** consists in the coupling of (±)-drimanoyl chloride ((±)-**3**) with lithiated and appropriately substituted aromatic synthons to furnish the ketones (±)-**7** and (±)-**17** which were reduced to the benzyl alcohols (±)-**8a**,**b** and (±)-**18a**,**b**, respectively (*Schemes 5*, *4*, and *12*). The 9,11-double bond of the drimenes (±)-**9** and (±)-**19** was formed by elimination of H_2O from the benzyl alcohols (±)-**8a**,**b** and (±)-**18a**,**b** (*Schemes 6* and *12*). New alternatives were applied to this elimination reaction involving either the pyridine·SO_3 complex or chloral as reagents.

Introduction. – Wiedendiol B (**1**) has been isolated from the marine sponge *Xestospongia wiedemayeri* [1]. The sesquiterpene arene **1** inhibits the cholesteryl ester transfer protein (CETP) [2]. This is a plasma neutral glycoprotein which mediates the net transfer of cholesteryl ester from high-density lipoprotein (HDL) into the low-density lipoprotein (LDL). Since low levels of HDL and high levels of LDL are directly correlated with increased coronary artery diseases, CETP may play a role in the pathogenesis of arteriosclerosis. The inhibition of CETP by compounds such as wiedendiol B (**1**) may be used to reduce the risks of coronary-artery disease.

Siphonodictyal B (**2**) and further siphonodictyals have been obtained from the burrowing sponge *Siphonodictyon coralliphagum* [3]. The mucus exudation in the oscular chimney of *S. coralliphagum* contains these sesquiterpene hydroquinones which are toxic against coral polyps. Thus, the overgrowth of the oscular chimneys by coral polyps is prevented. Siphonodictyal B (**2**) inhibits the growth of *Staphylococcus aureus* and *Bacillus subtilis.*



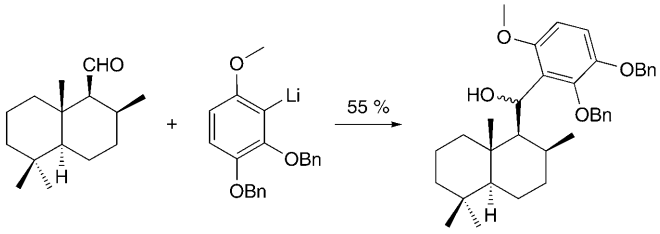
Wiedendiol B (**1**)



Siphonodictyal B (**2**)

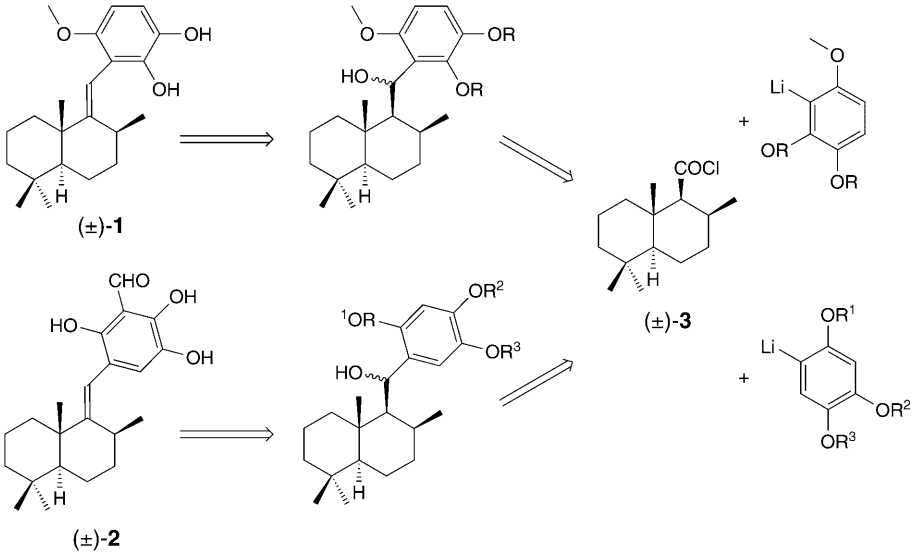
Wiedendiol B (**1**) has been synthesized before by *Barrero et al.* [4][5]. Starting from (−)-sclareol and (+)-*cis*-abienol, drimanal was obtained which was coupled with the lithiated 1,2-bis(benzyloxy)-4-methoxybenzene (*Scheme 1*). The instability of drimanal is probably the reason for the 55% yield of the coupling reaction.

Scheme 1. *Coupling of Drimanal with Lithiated 1,2-Bis(benzyloxy)-4-methoxybenzene*



Our *retro*-synthesis of (±)-wiedendiol B ((±)-**1**) and (±)-siphonodictyal B ((±)-**2**) leads to (±)-drimanoyl chloride ((±)-**3**) (*Scheme 2*). Coupling of (±)-**3** with the lithiated and protected aromatic synthons should give the aryl ketones which can be reduced to corresponding benzyl alcohols. Acid-catalyzed elimination of H_2O should give the desired 9,11-double bond. The drimanoyl chloride ((±)-**3**) was obtained from (±)-drimanic acid ((±)-**6**), which was prepared starting from *β*-ionone *via* a known route [6–8] with several steps being improved [9].

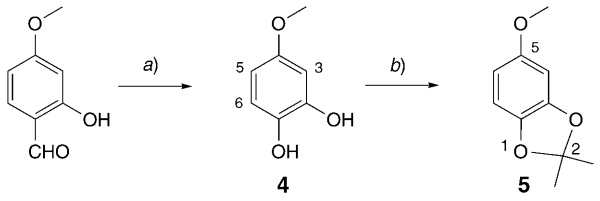
Scheme 2. retro-*Synthesis of (±)-Wiedendiol B* ((±)-**1**) *and (±)-Siphonodictyal B* ((±)-**2**)



Results and Discussion. – *Synthesis of (±)-Wiedendiol B* ((±)-**1**). The protected aromatic moiety of (±)-**1**, 5-methoxy-2,2-dimethyl-1,3-benzodioxole (**5**) was prepared by *Dakin* reaction of commercially available 2-hydroxy-4-methoxybenzaldehyde to obtain 4-methoxybenzene-1,2-diol (**4**) followed by generating the isopropylidene

group (*Scheme 3*), thus avoiding the problems and low yields of an already existing multi-step synthesis [10–12].

Scheme 3

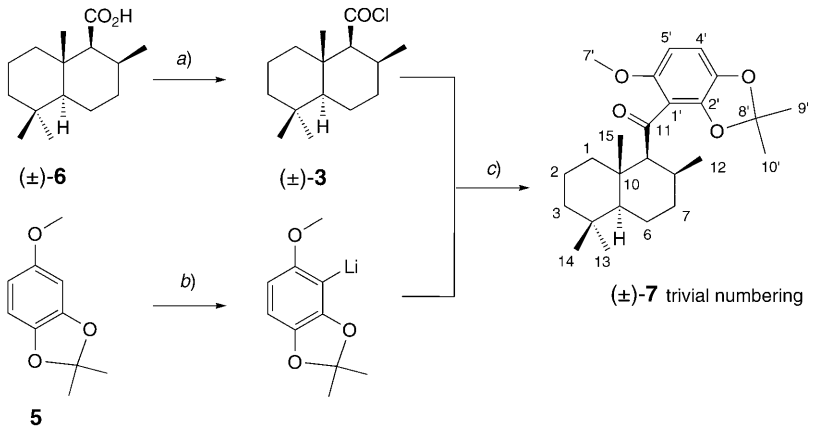


a) H_2O_2, NaOH; 100%. *b*) Me_2CO, benzene, TsOH; 82%.

(±)-Drimanic acid ((±)-**6**) was synthesized by catalytic hydrogenation of albicanic acid methyl ester (=methyl (1*RS*,4a*RS*,8a*RS*)-decahydro-5,5,8a-trimethyl-2-methylenenaphthalene-1-carboxylate) in presence of the *Wilkinson* catalyst followed by hydrolysis of the ester [13][14]. Although there is a published synthesis of drimanoyl chloride [15], this procedure is only suitable for a micro-scale synthesis and could not be transferred onto a preparative scale. Finally, we succeded to synthesize (±)-**3** in quantitative yield from (±)-**6** by using oxalyl chloride and catalytic amounts of dimethylformamide (DMF) (*Scheme 4*). For the coupling reaction, the aromatic compound **5** was lithiated with *t*-BuLi in THF at −18°, then a freshly prepared solution of (±)-drimanoyl chloride ((±)-**3**) was added giving the desired aryl ketone (±)-**7** in a good yield (82%). Although lithiated **5** was used in slight excess, no double coupling product could be detected. We assume that the sterical hindrance at the carbonyl group of (±)-**7** by the two large substituents is responsible (*Scheme 4*).

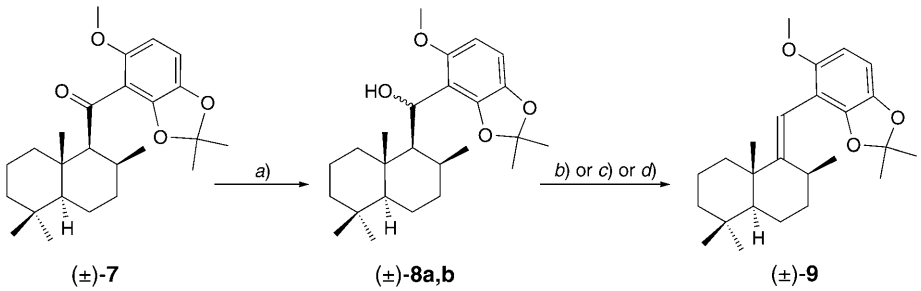
Reduction of the 11-carbonyl group of (±)-**7** by $LiBHEt_3$ yielded the diastereoisomeric benzyl alcohols (±)-**8a**,**b** in a very good yield (95%). To optimize the elimination step, it was necessary to try different reaction conditions (*Scheme 5*).

Scheme 4



a) $(COCl)_2$, cat. DMF; 100%. *b*) *t*-BuLi, THF, −18°; 100%. *c*) −18° to r.t., 3 h; 82%

Scheme 5



a) $LiBHEt_3$, THF; 95%. *b*) TsOH, benzene; 60%. *c*) Pyridine·SO_3, benzene; 98%. *d*) TsOH, chloral, benzene; 88%.

It has been reported that benzyl alcohols can be transformed into the corresponding styrenes by acid-catalyzed elimination of H_2O by using TsOH in benzene [4][5]. Due to the fact that the isopropylidene group of (±)-**8a**,**b** is not so stable under acidic conditions, we varied the reaction conditions. The results are summarized in *Table 1*. Standard conditions, *i.e.*, TsOH/benzene at room temperature, gave no conversion. Increase of the temperature resulted in low yields and decomposition at higher temperatures. Substitution of TsOH by the pyridine·SO_3 complex gave better results, although a higher reaction temperature was necessary for complete conversion. We assume that the benzylic OH group of (±)-**8a**,**b** reacts with the pyridine·SO_3 complex to an intermediate pyridinium sulfate ester which eliminates pyridinium hydrogen sulfate to give the desired styrene (±)-**9** in excellent yield (98%) (*Scheme 6*).

Scheme 6. *Possible Mechanism of the Elimination Step with the Pyridine·SO_3 Complex*

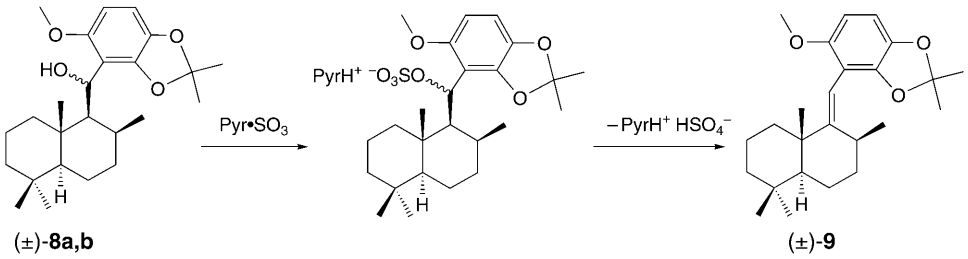


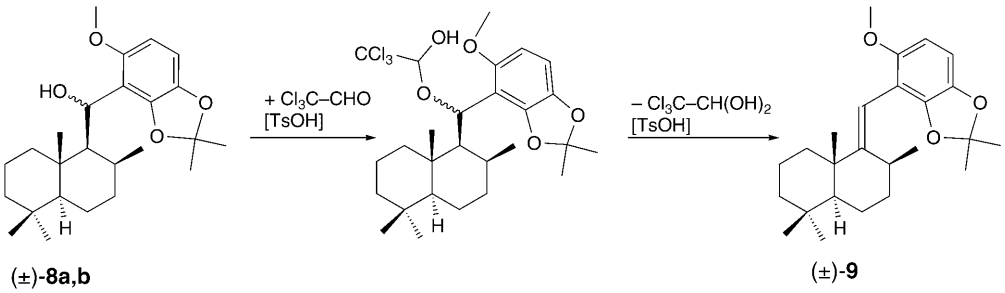
Table 1. *Elimination Reaction of the Benzyl Alcohol (±)*-**8a**,**b**

Reagent	Temperature	Reaction time	Results
TsOH·H_2O	r.t.	3/4 h	no conversion
	30°	22 h	yield 60%
	60°	1 h	decomposition
pyridine·SO_3	30°	45 h	incomplete conversion
	65°	4 h	yield 98%
chloral/TsOH·H_2O	35°	3 h	yield 88%

It is known that selective elimination reactions take place in the presence of 1,1,1-trichloro-3,3,3-trifluoroacetone (CCl_3COCF_3) and acid [16]. The selectivity of the elimination reaction with the halogenated acetone derivate is probably caused by an intermediate hemiketal formed by the alcohol and CCl_3COCF_3. Under acid catalysis, the hemiketal is selectively transformed to the product with an (*E*)-double bond. Due to the sterical hindrance at the benzyl alcohols (±)-**8a**,**b** and (±)-**18a**,**b**, only the (*E*)-configurated products (±)-**9** and (±)-**19** were formed (*Scheme 5* and below, *Scheme 12*). The ROESY cross peaks H–C(11) (δ 5.76)/H_{ax}-C(1) (δ 1.48) and H–C(11)/H_{eq}-C(1) (δ 1.92) of (±)-wiedendiol B ((±)-**1**) (*Scheme 8*) and H–C(11) (δ 6.12)/H_{ax}-C(1) (δ 1.48) and H–C(11)/H_{eq}-C(1) (δ 1.79) of the styrene (±)-**20** (see below, *Scheme 13*) confirmed the (*E*)-configuration of the 9,11 double bond.

We tried to substitute the expensive CCl_3COCF_3 by chloral (=2,2,2-trichloroethanal), assuming that chloral should react with the benzyl alcohol to a hemiacetal which can eliminate chloral hydrate to give a styrene. Indeed, the reaction of chloral with benzyl alcohol (±)-**8a**,**b** in the presence of TsOH led to styrene (±)-**9** in good yield (88%) (*Scheme 7*, *Table 1*). Furthermore, the reaction temperature could be considerably reduced as compared to the reaction in the presence of pyridine·SO_3 complex. This makes the elimination reaction in the presence of chloral to a good alternative elimination procedure in case of heat-sensitive substrates.

Scheme 7. *Possible Mechanism of the Elimination Step with Chloral*

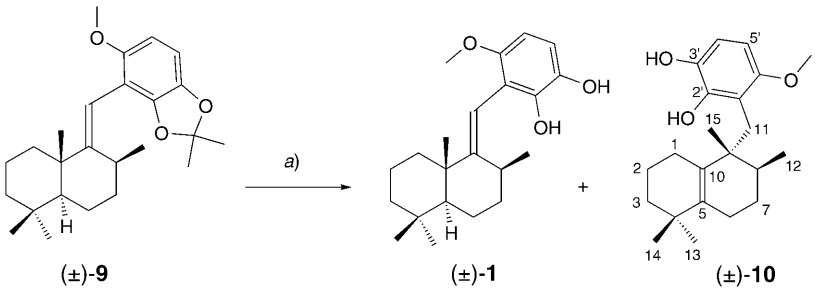


(±)-**8a**,**b** (±)-**9**

Finally, cleavage of the isopropylidene protection group under optimized conditions with HCl/EtOH at 65° yielded (±)-wiedendiol B ((±)-**1**; 65%) and the by-product (±)-**10** (15%) with a rearranged drimane skeleton (*Scheme 8*), similar to a by-product already reported for the elimination reaction in the synthesis of spongiaquinone [13]. The pseudoaxial α position at C(9) of the 2,3-dihydroxy-6-methoxybenzyl group of (±)-**10** was established by the ROESY cross peaks H_A-C(11) (δ 2.74)/H_{eq}-C(8) (δ 1.69) and H_B-C(11) (δ 2.96)/H_{eq}-C(8) and the NOEs between both H–C(11) protons and the pseudoequatorial β-positioned Me(15) moiety (δ 0.95). A comparison of the ^{1}H- and ^{13}C-NMR data of (±)-**10** with those of the by-product of the spongiaquinone synthesis showed some incorrect assignments. For that reason the correct NMR data of this compound are given in the *Exper. Part* (see there **22**).

Thus, we established a new synthesis of (±)-wiedendiol B ((±)-**1**) with a higher yield in the coupling reaction than already reported [4][5]. The new coupling–reduction–elimination method is also suitable for combinatorial syntheses.

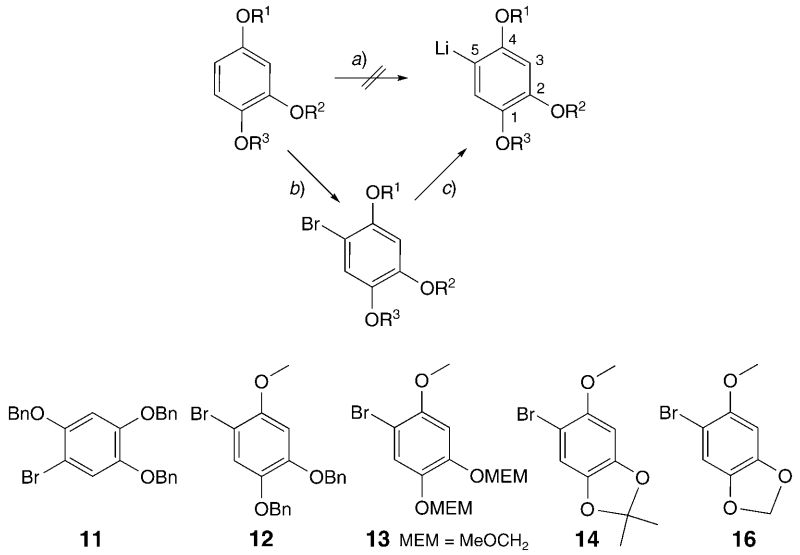
Scheme 8



a) HCl, EtOH; 65% of (±)-**1**, 15% of (±)-**10**.

Synthesis of Protected Siphonodictyal B ((±)-**21**). The *retro*-synthesis of (±)-siphonodyctyal B ((±)-**2**) led to (±)-drimanoyl chloride ((±)-**3**) and an aromatic compound with 1,2,4-trioxy substitution and, lithiation at C(5) (*Scheme 2*). To get the right coupling position, a direct lithiation is not possible. The aromatic compound would be lithiated at C(3) due to the strong coordinating *ortho*-effect of the oxy substituents at C(2) and C(4). Therefore, it was necessary to brominate firstly and then carry out a bromine–lithium exchange with BuLi (*Scheme 9*). Extensive studies revealed that the bromine–lithium exchange should be carried out at temperatures below $-100°$, otherwise a translithiation took place, and the coupling reaction gave a mixture of regioisomers. We used different aromatic bromo compounds, *i.e.* **11**–**14** and **16** (from **15**, see below), for the coupling with (±)-drimanoyl chloride ((±)-**3**).

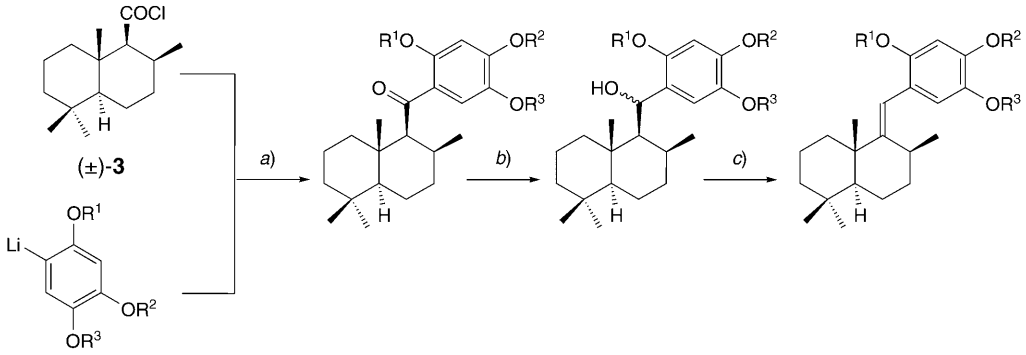
Scheme 9



a) BuLi. *b*) Br_2 or NBS. *c*) BuLi, $T \leq -100°$.

The coupling reactions with (±)-**3** were carried out as follows: The aromatic bromo compound was lithiated at −110° with BuLi. After 5 min, a freshly prepared solution of (±)-**3** was added and the mixture allowed to warm up to room temperature within *ca.* 2 h. The next step was the reduction of the corresponding aryl ketone with $LiBHEt_3$ followed by elimination of H_2O with TsOH (*Scheme 10*). The results of the coupling–reduction–elimination sequence are given in *Table 2*. This method showed good to excellent yields for coupling, reduction, and elimination. It has to be mentioned that, if R^1 = Me and $R^2 = R^3 = MeOCH_2$, one $MeOCH_2$-group (R^2) was split off during the elimination process (*Scheme 10*, *Table 2*).

Scheme 10



a) −110° to r.t. *b*) $LiBHEt_3$. *c*) TsOH, benzene.

Table 2. *Results of the Coupling–Reduction–Elimination Sequence Starting from (±)-***3** *and the Lithiated Derivatives Obtained from* **11**–**14** *and* **16**

	R^1	R^2	R^3	Coupling yield [%]	Reduction yield [%]	Elimination yield [%]
11	Bn	Bn	Bn	22	100	100
12	Me	Bn	Bn	47	100	75
13	Me	$MeOCH_2$	$MeOCH_2$	70	100	67[a])
14	Me	–CMe_2–		82	100	98
16	Me	–CH_2–		97	100	100

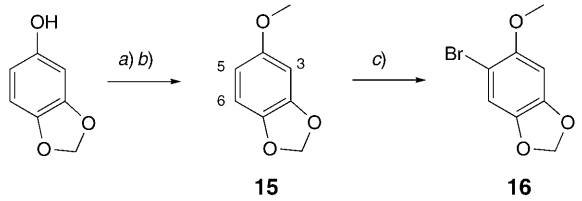
[a]) R^2 = H; the $MeOCH_2$ group was split off during the elimination process.

The best yield in the coupling–reduction–elimination sequence was achieved with 5-bromosesamyl methyl ether (=5-bromo-6-methoxy-1,3-benzodioxol; **16**). Compound **16** could easily be prepared by methylation of commercially available sesamol followed by bromination with Br_2 (95% over two steps) (*Scheme 11*).

After bromine–lithium exchange in **16**, the obtained 5-lithiated ether was coupled with (±)-drimanoyl chloride ((±)-**3**) to give aryl ketone (±)-**17** in excellent yield (97%) (*Scheme 12*). Reduction of (±)-**17** with $LiBHEt_3$ led to (±)-**18a**,**b** (100%). Elimination of H_2O from (±)-**18a**,**b** with TsOH gave (±)-**19** in quantitative yield.

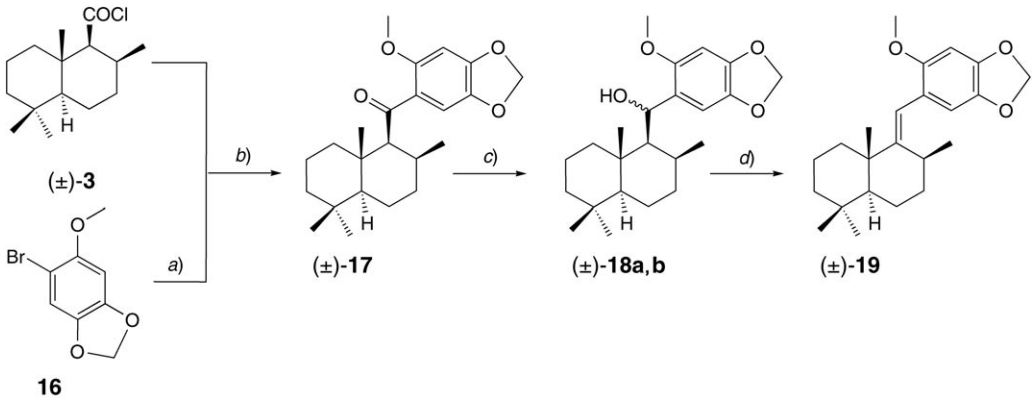
Formylation of (±)-**19** by lithiation followed by reaction with DMF gave the desired product (±)-**20** in good yield (85%) (*Scheme 13*). The methoxy group could easily be

Scheme 11



a) Et_4NOH. *b*) DMS; 100% from sesamol. *c*) Br_2, THF; 95%.

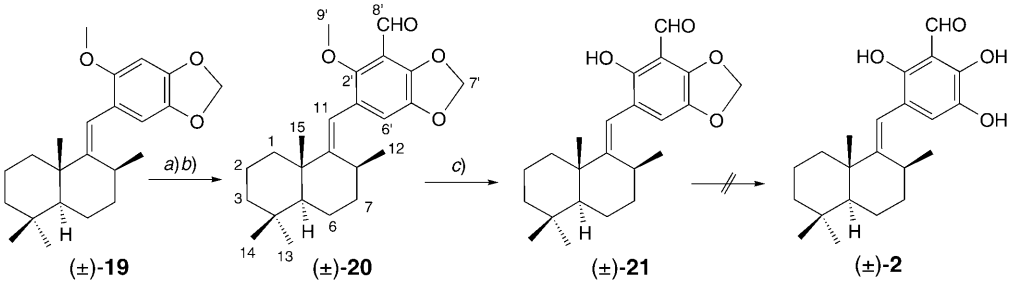
Scheme 12



a) BuLi, −110°. *b*) −110°–r.t.; 97% from (±)-**3**. *c*) $LiBHEt_3$; 100%. *d*) TsOH, benzene; 100%.

removed by treatment with BCl_3/Bu_4I to give (±)-**21** (76%). The methylenedioxy moiety was not affected. Unfortunately, our efforts to cleave the methylenedioxy group under different conditions (BX_3, X=Cl, Br, I; LiCl/quinoline, reflux; LiCl/DMF, reflux; NaSEt/DMF, reflux; $AlCl_3/CH_2Cl_2$, and others) were not successful, but a new and versatile reaction sequence for generating aromatic 9,11-drimenyl compounds as useful intermediates for the synthesis of sesquiterpene quinones and hydroquinones could be established.

Scheme 13



a) BuLi, TMEDA. *b*) DMF; 85% from (±)-**19**. *c*) BCl_3, Bu_4NI, CH_2Cl_2; 76%.

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Experimental Part

General. TLC: *Merck* silica gel *60 F_{254}* precoated plates; detection by 5% molybdophosphoric acid in EtOH (*Aldrich Chemicals, Ltd.*). Flash chromatography (FC): silica gel *Si 60* (40–63 μ; *Merck*). MPLC: *Labomatic-Laboprep*-MPLC unit *MD-50/80/100*. NMR: *Bruker AC-300*, *DRX-500*; δ in ppm, J in Hz; $CDCl_3$ as solvent and internal standard. MS: *Finnigan MAT 8500*, 70 eV; in m/z (rel.%).

1. *(±)-Wiedendiol B.* 1.1. *(±)-Drimanoyl Chloride (=(1*RS,*2*RS,*4a*RS,*8a*RS)*-Decahydro-2,5,5,8a-tetramethylnaphthalene-1-carbonyl Chloride*; (±)-**3**)). To a soln. of (±)-drimanic acid ((±)-**6**, 0.77 g, 3.23 mmol) in dry CH_2Cl_2 (40 ml), oxalyl chloride (2.77 ml, 32.30 mmol) and dry DMF (3 drops) were added. After 15 min at r.t., the mixture was heated under reflux for 30 min. The solvent was evaporated, the residue (0.83 g, 100%) dissolved in dry THF, and immediately used without further purification for the coupling reaction. ^{1}H-NMR (300 MHz): 2.77 (*d*, J=4.6, H–C(9)); 2.65 (H–C(8)); 1.84 (1 H–C(1)); 1.70 (2 H–C(7)); 1.60 (1 H–C(2)); 1.49 (1 H–C(6)); 1.39 (1 H–C(2)); 1.39 (1 H–C(6)); 1.37 (1 H–C(3)); 1.17 (*s*, Me(15)); 1.14 (1 H–C(3)); 1.08 (*d*, J=7.4, Me(12)); 1.03 (1 H–C(1)); 0.88 (*s*, Me(13)); 0.80 (*s*, Me(14)); 0.76 (H–C(5)). ^{13}C-NMR (75 MHz): 173.4 (C(11)); 73.0 (C(9)); 55.3 (C(5)); 41.8 (C(3)); 39.4 (C(1)); 39.2 (C(10)); 33.4 (C(7)); 33.4 (C(13)); 33.1 (C(4)); 30.8 (C(8)); 21.5 (C(14)); 17.9 (C(2)); 17.1 (C(6)); 16.9 (C(12)); 16.3 (C(15)).

4-Methoxybenzene-1,2-diol (**4**). To a mixture of 2-hydroxy-4-methoxybenzaldehyde (5.24 g, 34.44 mmol) and 30% H_2O_2 soln. (4.69 ml, 41.33 mmol) in THF/H_2O 5:1 (150 ml), NaOH (1.65 g, 41.25 mmol) in H_2O (20 ml) was added at r.t. After 1 h, conc. HCl soln. (pH *ca.* 2) and then H_2O were added, and the soln. was diluted with Et_2O. The org. layer was washed with $Na_2S_2O_3$ soln. and H_2O, filtered through silica gel/Na_2SO_4, and evaporated: 7.82 g (100%) of **4**. Red oil. R_f (hexane/AcOEt 1:1) 0.52. ^{1}H-NMR (300 MHz): 6.71 (*d*, J=8.7, H–C(6)); 6.44 (*d*, J=3.0, H–C(3)); 6.28 (*dd*, J=8.7, 3.0, H–C(5)); 3.67 (*s*, MeO). MS: 140 (100, M^+), 125 (81), 107 (24), 97 (11), 79 (15). HR-MS: 140.0473 ($C_7H_8O_3^+$; calc. 140.0473).

5-Methoxy-2,2-dimethyl-1,3-benzodioxole (**5**). A mixture of **4** (4.93 g, 35.23 mmol) and TsOH·H_2O (0.67 g, 3.52 mmol) in benzene/Me_2CO 5:1 (150 ml) was heated for 21 h under reflux under a water-separation funnel. The condensing solvent was dried with Na_2SO_4. After cooling to r.t., the mixture was filtered through *Alox B* (act. I) and evaporated: 5.81 g (82%) of **5**. Yellow oil. R_f (hexane/CH_2Cl_2 1:1) 0.42. ^{1}H-NMR (300 MHz): 6.60 (*d*, J=8.5, H–C(7)); 6.39 (*d*, J=2.5, H–C(4)); 6.26 (*dd*, J=8.5, 2.5, H–C(6)); 3.72 (*s*, MeO); 1.64 (*s*, 2 Me). MS: 180 (50, M^+), 165 (100), 140 (49), 125 (57), 43 (43), 40 (20). HR-MS: 180.0786 ($C_{10}H_{12}O_3^+$; calc. 180.0786).

*[(1*RS,*2*RS,*4a*RS,*8a*RS)*-Decahydro-2,5,5,8a-tetramethylnaphthalen-1-yl](5-methoxy-2,2-dimethyl-1,3-benzodioxol-4-yl)methanone* ((±)-**7**). A soln. of **5** (0.78 g, 4.33 mmol) in dry THF (30 ml) was treated with 1.5M *t*-BuLi in hexane (3.18 ml, 4.76 mmol) at −18°. After 15 min, freshly prepared (±)-**3** (0.83 g, 3.25 mmol) in dry THF (30 ml) was added, and the mixture was allowed to warm up to r.t. for 3 h. Sat. NH_4Cl soln. and Et_2O were added, and the org. layer was washed with H_2O and filtered through Na_2SO_4. The filtrate was evaporated and the residue purified by FC (silica gel, hexane/toluene 1:3): 1.06 g (82%) of (±)-**7**. Yellowish oil. R_f (toluene): 0.93. ^{1}H- and ^{13}C-NMR: *Table 3*. MS: 400 (14, M^+), 249 (39), 207 (100), 167 (33), 41 (28). HR-MS: 400.2614 ($C_{25}H_{36}O_4^+$; calc. 400.2614).

*(α*RS*)-α-[(1*RS,*2*RS,*4a*RS,*8a*RS)*- and (α*RS*)-α-[(1*SR,*2*SR,*4a*SR,*8a*SR)*-Decahydro-2,5,5,8a-tetramethylnaphthalen-1-yl]-5-methoxy-2,2-dimethyl-1,3-benzodioxole-4-methanol* ((±)-**8a**,**b**). To (±)-**7** (0.41 g, 1.02 mmol) in dry THF (30 ml), 1M $LiBHEt_3$ in THF (5.21 ml, 5.21 mmol) was added. After stirring for 1 h at r.t., sat. NH_4Cl soln., H_2O, and Et_2O were added. The org. layer was washed with brine, and filtered through Na_2SO_4, the filtrate evaporated, and the residue purified by FC (hexane/AcOEt 7:1): 0.39 g (95%) of (±)-**8a**,**b**. Colorless oil. R_f (hexane/AcOEt 7:1): 0.44. Since the product consists of two diastereoisomers, no further spectroscopic characterization was carried out.

*5-Methoxy-2,2-dimethyl-4-{[(1*E,*2*RS,*4a*RS,*8a*RS)*-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H)*-ylidene]methyl}-1,3-benzodioxole* ((±)-**9**). *Method A: Elimination with TsOH.* A mixture of (±)-**8a**,**b**

Table 3. *^{1}H- and ^{13}C-NMR Data of Compounds (±)-***7**, *(±)-***9**, *(±)-***10**, *and (±)-***1**. δ in ppm, coupling constants *J* in Hz. Trivial numbering, see *Schemes 4* and *8*.

	(±)-**7**[a])		(±)-**9**[a])		(±)-**10**[b])		(±)-**1**[b])	
	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)
CH_2(1)	38.8	0.98, 1.98	38.5	1.54, 1.84	27.5	1.76, 1.82	38.8	1.48, 1.92
CH_2(2)	18.2	1.34, 1.64	18.9	1.54, 1.71	19.6	1.51 (2 H)	18.8	1.56, 1.72
CH_2(3)	42.2	1.18, 1.37	42.1	1.27, 1.38	39.4	1.39, 1.47	42.0	1.20, 1.42
C(4)	33.2	–	34.0	–	34.6	–	34.0	–
H–C(5) or C(5)	56.4	0.82	54.6	1.03	138.7	–	55.1	0.98
CH_2(6)	17.5	1.46 (2 H)	17.8	1.54 (2 H)	21.5	2.01, 2.13	17.8	1.57 (2 H)
CH_2(7)	34.7	1.61 (2 H)	33.9	1.54 (2 H)	25.8	1.43, 2.07	34.2	1.49, 1.58
H–C(8)	30.8	2.24	32.3	2.73	37.0	1.69	32.0	2.57
H–C(9) or C(9)	65.6	2.99 (*d*, *J*=4.1)	158.9	–	42.1	–	164.1	–
C(10)	38.7	–	41.0	–	134.1	–	41.3	–
C(11), H–C(11) or CH_2(11)	203.8	–	109.4	5.78 (*s*)	36.0	2.74, 2.96 (2*d*, *J*=14.0)	109.1	5.76 (*s*)
Me(12)	17.2	1.03 (*d*, *J*=7.5)	21.9	1.08 (*d*, *J*=7.5)	15.6	0.81 (*d*, *J*=6.9)	21.9	1.01 (*d*, *J*=7.5)
Me(13)	33.5	0.83 (*s*)	33.0	0.88 (*s*)	27.9	1.05 (*s*)	33.4	0.90 (*s*)
Me(14)	21.6	0.83 (*s*)	21.8	0.88 (*s*)	28.8	0.99 (*s*)	21.8	0.89 (*s*)
Me(15)	16.9	1.29 (*s*)	22.5	1.20 (*s*)	22.4	0.95 (*s*)	22.8	1.22 (*s*)
C(1′)	116.2	–	112.5	–	116.4	–	114.8	–
C(2′)	145.7	–	145.3	–	142.9	–	139.8	–
C(3′)	142.0	–	141.4	–	139.0	–	137.9	–
H–C(4′)	108.2	6.59 (*d*, *J*=8.5)	104.7	6.49 (*d*, *J*=8.5)	111.8	6.70 (*d*, *J*=8.7)	112.6	6.74 (*d*, *J*=8.8)
H–C(5′)	102.5	6.22 (*d*, *J*=8.5)	102.4	6.23 (*d*, *J*=8.5)	103.1	6.35 (*d*, *J*=8.7)	102.7	6.33 (*d*, *J*=8.8)
C(6′)	151.8	–	152.9	–	152.0	–	151.0	–
Me(7′)	56.6	3.72 (*s*)	56.8	3.69 (*s*)	55.8	3.72 (*s*)	56.0	3.68 (*s*)
C(8′)	118.8	–	117.2	–	–	–	–	–
Me(9′)	25.6[c])	1.61 (*s*)[c])	25.6[c])	1.61 (*s*)[c])	–	–	–	–
Me(10′)	25.7[c])	1.64 (*s*)[c])	25.8[c])	1.63 (*s*)[c])	–	–	–	–
C(2′)–OH	–	–	–	–	–	5.90 (*s*)	–	5.10 (*s*)
C(3′)–OH	–	–	–	–	–	5.17 (*s*)	–	4.92 (*s*)

[a]) *AC-300* spectrometer. [b]) *DRX-500* spectrometer. [c]) Assignments may be reversed.

(0.11 g, 0.27 mmol) and $TsOH \cdot H_2O$ (20 mg, 0.13 mmol) in benzene (5 ml) was stirred at 30° for 22 h. The mixture was filtered through *Alox B* (act. I) and evaporated. The residue was purified by FC (silica gel, hexane/CH_2Cl_2 1:1): 60 mg (60%) of (±)-**9**. Colorless oil. R_f (hexane/CH_2Cl_2 1:1) 0.62. ^{1}H- and ^{13}C-NMR: *Table 3*. MS: 385 (22), 384 (73, M^+), 259 (30), 246 (100), 237 (69), 215 (35), 193 (46), 41 (38). HR-MS: 384.2664 ($C_{25}H_{36}O_3^+$; calc. 384.2664).

Method B: Elimination with Pyridine·SO$_3$ Complex. A mixture of (±)-**8a**,**b** (0.13 g, 0.32 mmol) and pyridine·SO_3 complex (0.81 g, 0.80 mmol) in benzene (10 ml) was stirred for 4 h at 65°. After filtration through *Alox B* (act. I), the solvent was evaporated: 0.12 g (98%) of (±)-**9**. Data of (±)-**9**: see above.

Method C: Elimination with Chloral/TsOH. A mixture of (±)-**8a**,**b** (0.11 g, 0.26 mmol), chloral (0.07 ml, 0.75 mmol), and $TsOH \cdot H_2O$ (20 mg, 0.13 mmol) in benzene (10 ml) was stirred at 35° for 3 h. The mixture was filtered through *Alox B* (act. I) and evaporated. The residue was purified by FC (silica gel, hexane/CH_2Cl_2 1:1): 90 mg (88%) of (±)-**9**. Colorless oil. Data of (±)-**9**: see above.

(±)-Wiedendiol B (=*4-Methoxy-3-{[(1*E,*2*RS,*4a*RS,*8a*RS*)-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H*)-ylidene]methyl}benzene-1,2-diol*; (±)-**1**) *and 4-Methoxy-3-{[(1*RS,*2*SR*)-1,2,3,4,5,6,7,8-octahydro-1,2,5,5-tetramethylnaphthalen-1-yl]methyl}benzene-1,2-diol* ((±)-**10**). Compound (±)-**9** (30 mg, 0.078 mmol) was treated with EtOH/HCl 7:1 (20 ml) at 50° for 21 h. The mixture was diluted with H_2O and Et_2O, the org. layer washed with H_2O, dried (Na_2SO_4), and evaporated. Further purification was carried out by MPLC (hexane/CH_2Cl_2 95:5 → 50:50, 60 min): 17 mg (65%) of (±)-**1** and 4 mg (15%) of (±)-**10**. Light yellow oils.

Data of (±)-**1**: R_f (CH_2Cl_2): 0.38. ^{1}H- and ^{13}C-NMR: *Table 3*. MS: 344 (27, M^+), 206 (31), 191 (100), 153 (50), 152 (39), 95 (23), 81 (23), 69 (43), 59 (42), 57 (21), 55 (54), 43 (50), 41(86). HR-MS: 344.2351 ($C_{22}H_{32}O_3^+$; calc. 344.2351).

Data of (±)-**10**: R_f (CH_2Cl_2): 0.25. ^{1}H- and ^{13}C-NMR: *Table 3*. MS: 344 (8, M^+), 192 (50), 191 (100), 190 (37), 153 (23), 135 (32), 121 (25), 109 (21), 95 (25), 69 (24). HR-MS: 344.2351 ($C_{22}H_{32}O_3^+$; calc. 344.2351).

2. *Protected (±)-Siphonodictyal B. Sesamol Methyl Ether* (=*5-Methoxy-1,3-benzodioxole*; **15**). Sesamol (5.47 g, 39.60 mmol) was treated with 1.5M Et_4NOH (39.6 ml, 59.40 mmol) in MeOH. After evaporation, the residue was dissolved in THF (150 ml), the soln. cooled to 0°, DMS (38.42 ml, 396.05 mmol) added, and then the mixture stirred at r.t. for 1 h. The mixture was hydrolyzed with conc. NH_3 soln./H_2O/ice 1:1:1, and the diluted with Et_2O and H_2O and the org. layer washed with H_2O, dried (Na_2SO_4), and evaporated: 6.16 g (100%) of **15**. Yellowish oil. R_f (hexane/AcOEt 4:1) 0.77. ^{1}H-NMR (300 MHz): 6.64 (*d*, *J* = 8.5, H–C(6)); 6.42 (*d*, *J* = 2.5, H–C(3)); 6.25 (*dd*, *J* = 8.5, 2.5, H–C(5)); 5.84 (*s*, OCH_2O); 3.68 (*s*, MeO). MS: 152 (98, M^+), 137 (100), 107 (41), 79 (42), 53 (22), 51 (20). HR-MS: 152.0473 ($C_8H_8O_3^+$; calc. 152.0473).

5-Bromosesamol Methyl Ether (=*5-Bromo-6-methoxy-1,3-benzodioxol*; **16**). A soln. of **15** (1.08 g, 7.10 mmol) in dry THF (100 ml) was treated with Br_2 (0.36 ml, 7.10 mmol) at 0°. After stirring for 5 min at 0°, Et_2O and sat. Na_2CO_3 soln. were added. The org. layer was separated, washed with H_2O and brine, filtered through Na_2SO_4 and evaporated: 1.55 g (95%) of **16**. White solid. R_f (toluene): 0.72. ^{1}H-NMR (300 MHz): 6.93 (*s*, H–C(6)); 6.50 (*s*, H–C(3)); 5.88 (*s*, OCH_2O); 3.76 (*s*, MeO). MS: 232 (100, M^+), 230 (93), 217 (77), 215 (77), 187 (27). HR-MS: 229.9579 ($C_8H_7BrO_3^+$; calc. 229.9579).

*[(1*RS,*2*RS,*4a*RS,*8a*RS*)-Decahydro-2,5,5,8a-tetramethylnaphthalen-1-yl](6-methoxy-1,3-benzodioxol-5-yl)methanone* ((±)-**17**). A soln. of **16** (1.00 g, 4.36 mmol) in dry THF (50 ml) was cooled to −110° and treated with 1.6M BuLi in hexane/cyclohexane (2.73 ml, 4.36 mmol). After 5 min, a freshly prepared soln. of (±)-**3** (2.18 mmol) in dry THF (20 ml) was added dropwise. The mixture was allowed to warm up to r.t. for *ca.* 1.5 h, and sat. NH_4Cl soln. (2.0 ml) was added. For purification, the mixture was adsorbed on silica gel and submitted to FC (hexane/toluene 1:1 for the eluation of **15** and **16**, then hexane/AcOEt 7:1): 0.79 g (97%) of (±)-**17**. Yellow oil. R_f (hexane/Me_2CO 3:1): 0.67. ^{1}H- and ^{13}C-NMR: *Table 4*. MS: 372 (13, M^+), 221 (34), 194 (16), 180 (10), 179 (100). HR-MS: 372.2300 ($C_{23}H_{32}O_4^+$; calc. 372.2301).

*(α*RS*)-α-[1*RS,*2*RS,*4a*RS,*8a*RS*)- and (α*RS*)-α-[(1*SR,*2*SR,*4a*SR,*8a*SR*)-Decahydro-2,5,5,8a-tetramethylnaphthalen-1-yl]-6-methoxy-1,3-benzodioxol-5-methanol* ((±)-**18a**,**b**). To a soln. of (±)-**17** (0.31 g, 0.83 mmol) in dry THF (100 ml), 1.0M $LiBHEt_3$ in THF (4.16 ml, 4.16 mmol) was added at 0°. After stirring at r.t. for 1 h, sat. NH_4Cl soln. was added, the mixture stirred for additional 5 min and diluted with Et_2O/H_2O. The org. layer was washed with H_2O, filtered through Na_2SO_4, and evaporated. The residue was further purified by FC (hexane/Me_2CO 3:1): 0.31 g (100%) of (±)-**18a**,**b**. Yellow wax. R_f (hexane/Me_2CO 3:1) 0.54. Since the product consists of two diastereoisomers, no further spectroscopic characterization was carried out.

*6-Methoxy-5-{[(2*RS,*4a*RS,*8a*RS*)-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H*)-ylidene]methyl}-1,3-benzodioxole* ((±)-**19**). A soln. of (±)-**18a**,**b** (0.31 g, 0.83 mmol) in benzene (20 ml) was treated with $TsOH \cdot H_2O$ (0.16 g, 0.83 mmol) at r.t. for 1 h. The mixture was diluted with sat. Na_2CO_3 soln., Et_2O, and H_2O. The org. layer was washed twice with sat. Na_2CO_3 soln. and H_2O, dried (Na_2SO_4), and evaporated:

Table 4. *[1]H- and [13]C-NMR Data of Compounds (±)-***17**, *(±)-***19**, *(±)-***20**, and *(±)-***21**. δ in ppm, coupling constants *J* in Hz. Trivial numbering, see *Scheme 13*

	(±)-**17**[a])		(±)-**19**[a])		(±)-**20**[a])		(±)-**21**[a])	
	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)
CH_2(1)	39.4	0.90, 1.79	38.6	1.51, 1.76	38.7	1.48, 1.79	38.5	1.52, 1.79
CH_2(2)	18.2	1.30, 1.61	18.9	1.54, 1.71	18.8	1.57, 1.71	18.9	1.56, 1.69
CH_2(3)	42.2	1.13, 1.34	42.1	1.19, 1.39	42.1	1.18, 1.42	42.0	1.21, 1.38
C(4)	33.2	–	34.0	–	34.0	–	33.9	–
H–C(5)	56.6	0.83	54.6	1.00	54.9	0.94	54.5	1.03
CH_2(6)	17.6	1.46 (2 H)	17.8	1.51, 1.60	17.7	1.47, 1.61	17.8	1.49, 1.67
CH_2(7)	34.5	1.62 (2 H)	34.1	1.51 (2 H)	34.1	1.47, 1.59	34.0	1.55 (2 H)
H–C(8)	30.6	2.20	30.8	2.98	31.1	2.92	31.1	2.91
H–C(9) or C(9)	64.1	3.24 (*d*, *J* = 4.0)	156.0	–	158.0	–	158.0	–
C(10)	38.7	–	40.9	–	41.0	–	41.0	–
C(11), H–C(11)	204.8	–	115.1	6.10 (*s*)	114.1	6.12 (*s*)	113.3	6.08 (*s*)
Me(12)	17.0	0.97 (*d*, *J* = 7.5)	22.6	1.20 (*d*, *J* = 7.3)	22.4	1.20 (*d*, *J* = 7.4)	22.5	1.20 (*d*, *J* = 7.4)
Me(13)	33.6	0.84 (*s*)	33.4	0.86 (*s*)	33.4	0.87 (*s*)	33.3	0.86 (*s*)
Me(14)	21.6	0.83 (*s*)	21.8	0.87 (*s*)	21.8	0.88 (*s*)	21.8	0.87 (*s*)
Me(15)	16.8	1.28 (*s*)	22.8	1.18 (*s*)	22.5	1.18 (*s*)	22.9	1.18 (*s*)
C(1′)	124.6	–	121.1	–	125.7	–	119.1	–
C(2′)	154.2	–	152.6	–	154.2	–	152.7	–
H–C(3′) or C(3′)	94.7	6.48 (*s*)	95.3	6.50 (*s*)	114.2	–	106.6	–
C(4′)	150.6	–	146.2	–	146.1	–	148.3	–
C(5′)	141.5	–	140.7	–	144.2	–	139.6	–
H–C(6′)	109.0	6.94 (*s*)	109.7	6.65 (*s*)	115.1	6.80 (*s*)	117.6	6.89 (*s*)
CH_2(7′)	101.7	5.93 (*s*)	100.9	5.87 (*s*)	102.9	6.07 (*s*)	102.4	6.02 (s)
H–C(8′)	–	–	–	–	188.7	10.26 (*s*)	191.3	10.10 (*s*)
Me(9′)	56.7	3.80 (*s*)	56.9	3.72 (*s*)	62.7	3.75 (*s*)	–	–
OH–C(2′)	–	–	–	–	–	–	–	10.69 (*s*)

[a]) *DRX-500* spectrometer.

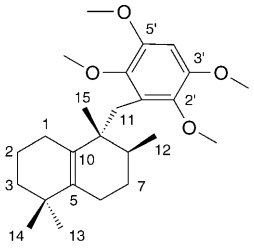
0.29 g (100%) of (±)-**19**. Colorless solid. R_f (hexane/AcOEt 7:1) 0.79. ^{1}H- and ^{13}C-NMR: *Table 4*. MS: 356 (75, M^+), 231 (62), 218 (82), 191 (49), 189 (31), 187 (34), 179 (26), 165 (100), 95 (25), 69 (30), 43 (39), 41 (31), 32 (62). HR-MS: 356.2353 ($C_{23}H_{32}O_3^+$; calc. 356.2351).

*5-Methoxy-6-{[(1*E*,2*RS*,4a*RS*,8a*RS*)-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H*)-ylidene]-methyl}-1,3-benzodioxole-4-carboxaldehyde* ((±)-**20**). To a mixture of (±)-**19** (1.00 g, 2.81 mmol) and *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine (TMEDA; 0.51 ml, 3.37 mmol) in dry THF (50 ml), 1.6M BuLi in hexane (2.11 ml, 3.37 mmol) was added at −20°. After stirring for 10 min, dry DMF (1.09 ml, 14.05 mmol) was added. The mixture was allowed to warm up to r.t., and sat. NH_4Cl soln. (3 ml) was added. After stirring for 5 min, the mixture was adsorbed on silica gel and submitted to FC (hexane/AcOEt 7:1): 0.92 g (85%) of (±)-**20**. Yellow wax. R_f (hexane/AcOEt 7:1): 0.31. ^{1}H- and ^{13}C-NMR: *Table 4*. MS: 384 (52, M^+), 246 (100), 215 (59), 193 (44), 191 (30). HR-MS: 384.2301 ($C_{24}H_{32}O_4^+$; calc. 384.2301).

*5-Hydroxy-6-{[(1*E*,2*RS*,4a*RS*,8a*RS*)-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H*)-ylidene]methyl}-1,3-benzodioxole-4-carboxaldehyde* ((±)-**21**). A mixture of (±)-**20** (79 mg, 0.21 mmol) and Bu_4NI (0.27 g, 0.72 mmol) in dry CH_2Cl_2 (20 ml) was treated with 1.0M BCl_3 in hexane (0.72 ml, 0.72 mmol) at −78°. After warming up for 2 h to r.t., H_2O was added, and the mixture was stirred for additional 10 min. Et_2-

O/H_2O was added, the org. layer washed with H_2O (3 times), dried (Na_2SO_4), and evaporated. Further purification was carried out by FC (hexane/toluene 1:1): 58 mg (76%) of (±)-**21**. Yellow oil. R_f (hexane/AcOEt 4:1): 0.57. ^{1}H- and ^{13}C-NMR: *Table 4*. MS: 370 (44, M^+), 245 (24), 233 (21), 232 (100), 217 (35), 191 (36), 55 (33), 43 (21), 41 (37). HR-MS: 370.2144 ($C_{23}H_{30}O_4^+$; calc. 370.2144).

*(1*RS*,2*SR*)-1,2,3,4,5,6,7,8-Octahydro-1,2,5,5-tetramethyl-1-[(2,3,5,6-tetramethoxyphenyl)methyl]-naphthalene* ((±)-**22**). ^{1}H-NMR (360 MHz; trivial numbering): 6.42 (H–C(4′)); 3.83 (MeO–C(3′), MeO–C(5′)); 3.70 (MeO–C(2′), MeO–C(6′)); 2.77 (*d*, *J* = 12.8, H_B–C(11)); 2.64 (*d*, *J* = 12.8, H_A–C(11)); 2.15 (1 H–C(1)); 2.11 (1 H–C(7)); 2.01 (1 H–C(6)); 1.89 (1 H–C(1)); 1.87 (1 H–C(6)); 1.79 (H–C(8)); 1.61 (2 H–C(2)); 1.43 (1 H–C(3)); 1.39 (1 H–C(7)); 1.37 (1 H–C(3)); 1.02 (*s*, Me(13)); 0.95 (*s*, Me(14)); 0.73 (*s*, Me(15)); 0.68 (*d*, *J* = 6.9, Me(12)). ^{13}C-NMR (90 MHz): 148.6 (C(3′), C(5′)); 142.2 (C(2′), C(6′)); 134.1 (C(5)); 132.4 (C(10)); 128.3 (C(1′)); 96.7 (C(4′)); 60.1 (MeO–C(2′), MeO–C(6′)); 55.9 (MeO–C(3′), MeO–C(5′)); 42.6 (C(9)); 40.1 (C(3)); 34.2 (C(4)); 33.1 (C(8)); 32.9 (C(11)); 28.9 (C(14)); 27.8 (C(13)); 26.3 (C(1)); 25.8 (C(7)); 20.6 (C(6)); 20.2 (C(2)); 20.1 (C(15)); 15.1 (C(12)).



(±)-**22** trivial numbering

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