Total Synthesis of the Marine Sesquiterpene Quinones Hyatellaquinone and Spongiaquinone

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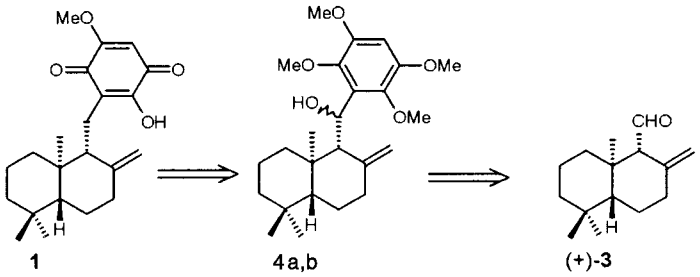
The synthesis of the marine sesquiterpene quinone (+)-hyatellaquinone (**1**) was achieved starting from the sesquiterpene aldehyde (+)-albicanal ((+)-**3**) (*Schemes 3* and *4*). Coupling of (+)-albicanal with 2,3,5,6-tetramethoxyphenyllithium led to the aryl-sesquiterpene system, which was modified to the target molecule. Furthermore, the first total synthesis of the marine compound spongiaquinone (**2**) was carried out starting from ((−)-albicanal (−)-**3**) in a reaction sequence encompassing a stereoselective C=C bond hydrogenation and a one-pot AcOH elimination/demethylation reaction (*Schemes 7* and *10*). The occurrence of 1,2- and 1,4-benzoquinone forms of **1** and **2** depends on the pH of the solvent system.

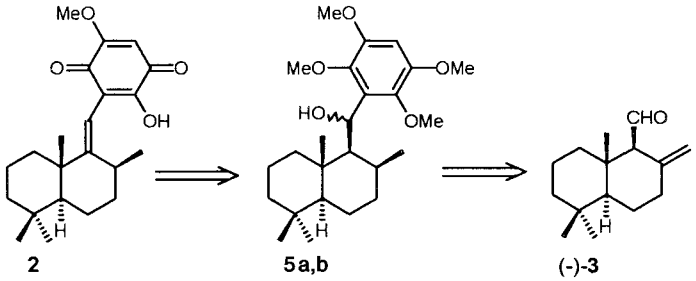
Introduction. – The sesquiterpene quinone hyatellaquinone has been isolated from the alga *Peyssonnelia* sp. and the marine sponges *Hyatella intestinalis* [1] and *Spongia* sp. [2]. Spongiaquinone has been obtained from the sponges *Spongia* sp. [2] and *Stelospongia conulata* [3]. Sesquiterpene quinones with a 6-hydroxy-3-methoxy-1,4-benzoquinone moiety like ilimaquinone or mamanuthaquinone show antitumor activity, inhibition of the HIV1 reverse transcriptase, and immunomodulation [4–7]. Thus, hyatellaquinone and spongiaquinone are attractive candidates for pharmacological testing. Therefore, we intended to develop an effective synthesis for these compounds. The absolute configuration of naturally occurring (+)-(5*R*,9*R*,10*R*)-hyatellaquinone[1]) (**1**) was recently established: a synthesis starting from the commercially available synthon (+)-sclareolide led to (−)-(5*S*,9*S*,10*S*)-hyatellaquinone [8]. Herein we describe the synthesis of (+)-hyatellaquinone (**1**) *via* (+)-albicanal (=(+)-albicanaldehyde; (+)-**3**) (*Scheme 1*). Moreover, the first total synthesis of spongiaquinone (**2**) was achieved starting from (−)-albicanal ((−)-**3**) (*Scheme 2*). The

Scheme 1. retro*Synthesis of* **1** *Led to (+)-Albicanal* ((+)-**3**)



[1]) Sesquiterpene numbering; for systematic names, see *Exper. Part.*

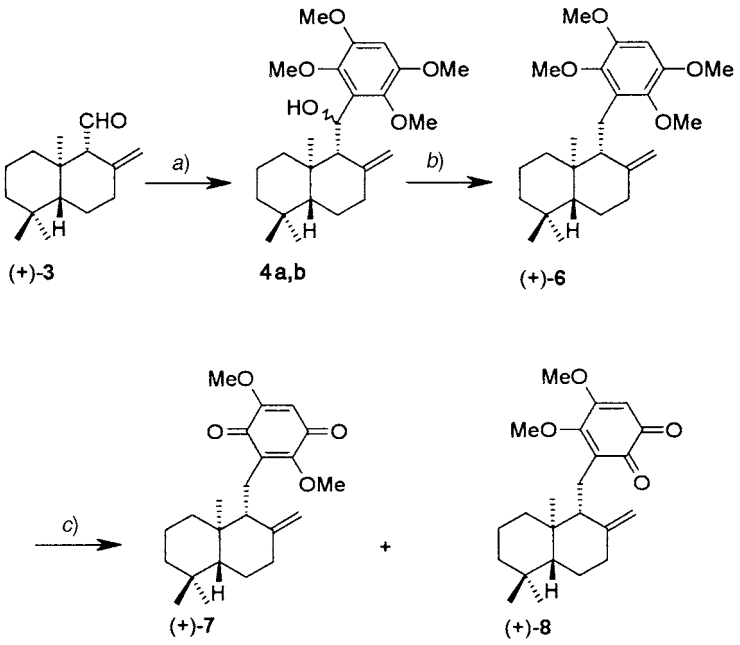
Scheme 2. retro-*Synthesis of* **2** *Led to (−)-Albicanal* ((−)-**3**)



necessary aldehydes (+)- and (−)-albicanal ((+)- and (−)-**3**, resp.) were obtained from (+)- and (−)-albicanic acid, which were prepared starting from β-ionone *via* a known route [9–11]. Several steps of this procedure were improved [12].

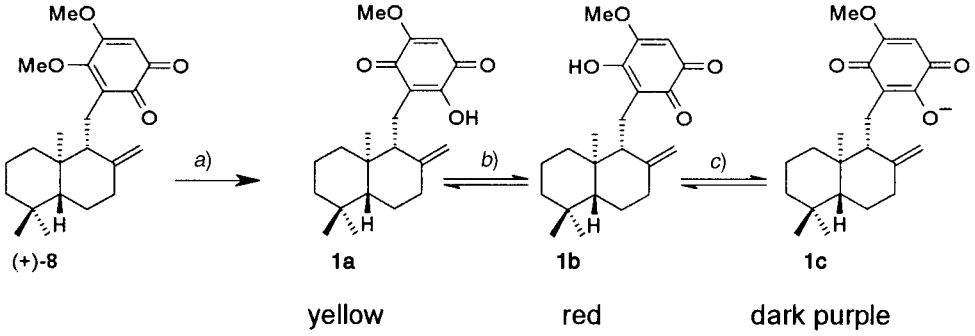
Results and Discussion. – *Synthesis of Hyatellaquinone* (**1**). – (+)-Albicanal ((+)-**3**) was coupled with 2,3,5,6-tetramethoxyphenyllithium (*Scheme 3*) to give the benzylic alcohols **4a**,**b** as a mixture of diastereoisomers, which were deoxygenated to (+)-**6** [12]. Oxidation of (+)-**6** with $Ce(NH_4)_2(NO_3)_6$ in $MeCN/H_2O$ under various standard conditions [8][13] gave erratic results. However, (+)-**6** was oxidized with Ce(N-

Scheme 3



a) 2,3,5,6-Tetramethoxyphenyllithium (1.2 equiv.), THF, −78° (85%). *b*) 1. Li (25 equiv.), NH_3/THF, −78°; 2. NH_4Cl (80%). *c*) $Ce(NH_4)_2(NO_3)_6$ (5 equiv.) in H_2O/MeCN, MeCN/DMF (24% of (+)-**7**; 34% of (+)-**8**).

Scheme 4

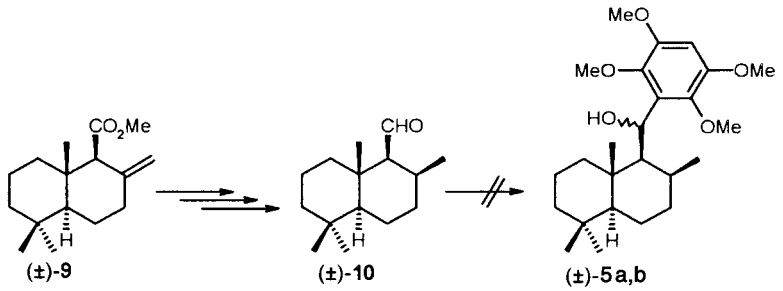


a) $HClO_4$, $MeCN/H_2O$ (99%). *b*) pH 5.2. *c*) pH 5.6.

$H_4)(NO_3)_6$ in $MeCN/DMF/H_2O$ to the 1,4-benzoquinone (+)-**7** (24%) and the 1,2-benzoquinone (+)-**8** (34%). Demethylation of the red 1,2-benzoquinone (+)-**8** with $HClO_4$ in $MeCN/H_2O$ yielded the yellow title compound **1a** (=**1**; *Scheme 4*). The increase of the pH above 5.2 led to a color change to intense red, corresponding to the structure **1b**. Increasing the pH to above 5.6 resulted in a dark purple solution containing the corresponding anion **1c** and its mesomeric forms. The interconversion of these three substances is reversible. A similar isomerization of the sesquiterpene quinone ilimaquinone with the same 1,4-benzoquinone moiety has already been reported [14]. A comparison of optical rotation and spectroscopic data (MS, NMR) of **1a** with the published data of the natural (+)-hyatellaquinone (**1**) [1][2] showed good agreement.

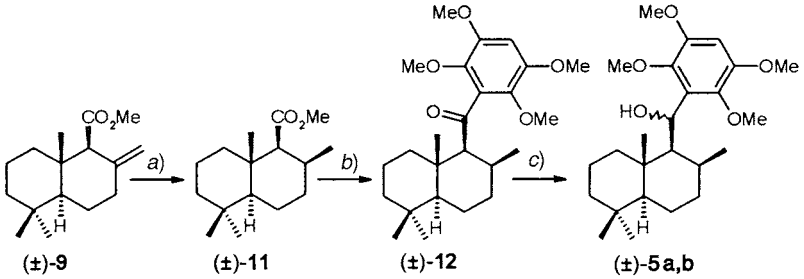
Synthesis of Spongiaquinone (**2**). The coupling reaction of drimanal ((±)-**10**) with 2,3,4,5-tetramethoxyphenyllithium was not successful due to the instability of (±)-**10** (*Scheme 5*). Thus, we looked for another method to synthesize the benzyl alcohols (±)-**5a**,**b**.

Scheme 5. *Unsuccessful Coupling of Drimanal* ((±)-**10**) *with 2,3,4,5-Tetramethoxyphenyllithium*



Coupling of (±)-drimanic acid methyl ester ((±)-**11**) with 2,3,4,5-tetramethoxyphenyllithium (*Scheme 6*) yielded ketone (±)-**12** (33%). Ester (±)-**11** could be reisolated (57%). Varying the reaction conditions did not improve the yield of (±)-**12**. Reduction of the exocyclic carbonyl group with DIBAL (diisobutylaluminium hydride)

Scheme 6

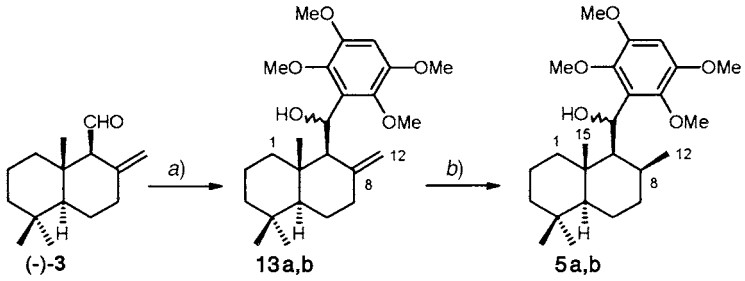


a) [RhCl(PPh$_{3)3}$], H_2, C_6H_6/MeOH 2 :1 (84%). *b*) 2,3,5,6-Tetramethoxyphenyllithium (2 equiv.), THF, 0° (33% of (±)-**12**, 57% of (±)-**11**. *c*) DIBAL (5 equiv.), CH_2Cl_2, 0° (95%).

led to the diastereoisomeric benzyl alcohols (±)-**5a**,**b** in a very good yield (95%). Unfortunately, the overall yield of (±)-**5a**,**b** starting from albicanic acid methyl ester ((±)-**9**) was only 26%.

A successful strategy for the synthesis of **5a**,**b** based on the coupling of (−)-albicanal ((−)-**3**) with 2,3,5,6-tetramethoxyphenyllithium to **13a**,**b** under the conditions described above (*Scheme 7*). The exocyclic $CH_2(12)$=C(8) bond of the benzyl alcohols **13a**,**b** should be stereoselectively hydrogenated to **5a**,**b** with (8*S*) configuration[1]). Since the first attempt of hydrogenation with [RhCl(PPh_3)$_3$] as catalyst failed, we tried the hydrogenation in presence of Pd/C. Stirring a solution of **13a**,**b** under H_2 in MeOH/AcOEt 5 :2 over Pd/C for 1 h at room temperature yielded the benzyl alcohols **5a**,**b** (94%). The axial configuration of Me−C(8) of **5a**,**b** was established by NOESY (cross-peak Me(12)/Me(15)).

Scheme 7

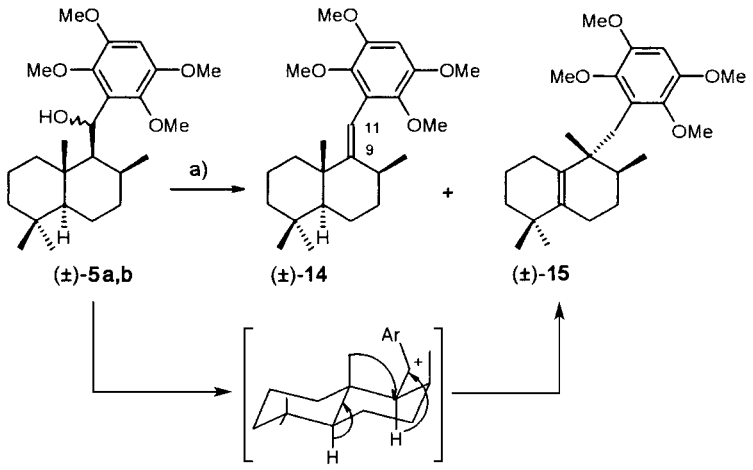


a) 2,3,5,6-Tetramethoxyphenyllithium (1.2 equiv.), THF, −78° (85%). *b*) Pd/C, H_2, MeOH/AcOEt 5 :2 (94%).

The exocyclic (*E*)-C(9)=CH(11)[1]) bond in (±)-**14** was introduced by an acid-catalyzed elimination of H_2O from (±)-**5a**,**b** in the presence of 1,1,1-trichloro-3,3,3-trifluoropropan-2-one [15] (*Scheme 8*). To our surprise, a second compound (±)-**15** was obtained, which was formed by an unusual drimane-skeleton rearrangement. The skeleton rearrangement of (±)-**5a**,**b** could be explained as follows: The benzylic OH group of (±)-**5a**,**b** reacts with 1,1,1-trichloro-3,3,3-trifluoropropan-2-one to a hemiketal that generates, during its acid-catalyzed transformation, a benzylic carbocation. The

latter can react in two different ways: proton elimination from position 9 leads to the desired elimination product (±)-**14**, whereas hydride shift from position 9 to the cation center C(11) followed by the shift of Me(15) to position 9 and elimination of H–C(5) results in compound (±)-**15** (*Scheme 8*). It is known that aryl-sesquiterpenes bearing a Me group in the α-position to a C=C bond can undergo acid-catalyzed rearrangement including Me-group shifts [14]. Efforts to suppress rearrangement (±)-**5a**,**b** → (±)-**15** by replacing TsOH with pyridinium tosylate did not have the desired effect; only the reaction time was increased.

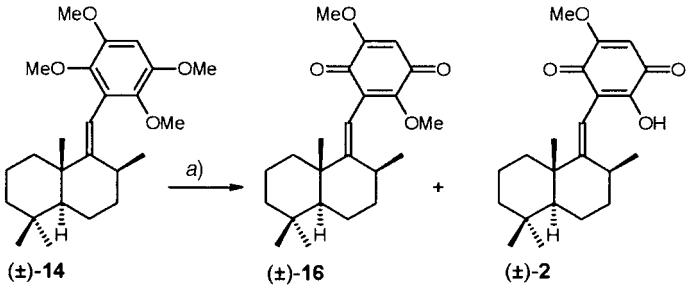
Scheme 8



a) 1,1,1-Trichloro-3,3,3-trifluoropropan-2-one (3 equiv.). TsOH, C_6H_6 (30% of (±)-**14**, 38% of (±-**15**).

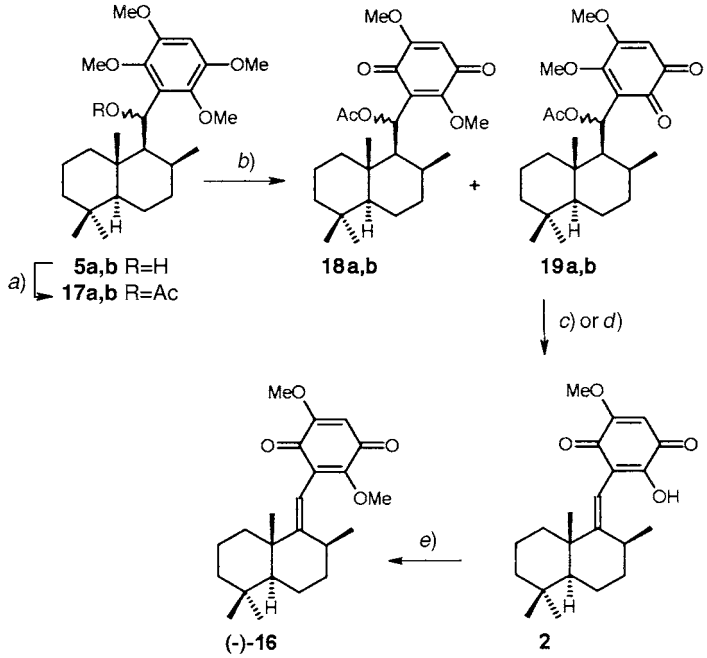
Before optimizing the elimination process from **5a**,**b**, we checked the next reaction step, the oxidation of (±)-**14** (*Scheme 9*). $Ce(NH_4)_2(NO_3)_6$ Oxidation of (±)-**14**, carried out as described above for the synthesis of (+)-hyatellaquinone (**1**), did not result in the desired dimethoxy-1,2-benzoquinone; only the isomeric dimethoxy-1,4-benzoquinone (±)-**16** could be isolated in 30% yield. Unexpectedly, we were able to isolate 4% of (±)-spongiaquinone ((±)-**2**). As the C(9)=C(11)[1]) bond seemed to disturb the oxidation process, we used another strategy: protection of the benzylic OH group of **5a**,**b** by acetylation followed by oxidation of **17a**,**b** with $Ce(NH_4)_2(NO_3)_6$ (*Scheme 10*). Acetylation under various standard conditions (*N*,*N*-dimethylpyridin-4-amine (DMAP), pyridine, Ac_2O, 24 h, room temperature) gave no turnover. Finally, acetylation could be achieved under more-vigorous reaction conditions (DMAP, pyridine, Ac_2O, 4 h, reflux) in 78% yield. Oxidation of the benzylic alcohols **17a**,**b** gave, besides the desired dimethoxybenzoquinones **18a**,**b** and **19a**,**b** (yields 5 and 50% respectively), also 4% of spongiaquinone (**2**). Treatment of the dimethoxy-1,2-benzoquinone **19a**,**b** with acid ($HClO_4$, TsOH) led to elimination of AcOH and demethylation at position 6′. The use of TsOH gave a higher yield (74%) in comparison with $HClO_4$ (48%). As described before [2], optical-rotation measurement of spongiaquinone (**2**) is impossible. Thus, **2** was transformed into spongiaquinone methyl ether ((–)-**16**). A comparison of the spectroscopic data (NMR, MS) of **2** and optical

Scheme 9



a) $Ce(NH_4)_2(NO_3)_4$ in (5 equiv.) H_2O/MeCN, MeCN/DMF 1:1, $HClO_4/H_2O$ (30% of (±)-**16**, 4% of (±)-**2**).

Scheme 10



a) DMAP (0.2 equiv.), Py, Ac_2O (10 equiv.), 4 h, reflux (78% of **17a**,**b**). *b*) $Ce(NH_4)_2(NO_3)_6$ (5 equiv.) in H_2O/MeCN, MeCN/DMF 2:1 (5% of **18a**,**b**, 50% of **19a**,**b**. *c*) $HClO_4/H_2O$, MeCN (48%). *d*) $TsOH \cdot H_2O$ (2 equiv.), benzene (74%). *e*) MeI (excess), Me_2CO, K_2CO_3.

rotation of (−)-**16** with natural spongiaquinone and its methyl ether [2][3] showed good agreement. The pH-depending isomerization of the benzoquinone moiety of **2** is the same as that described above for (+)-hyatellaquinone (**1**) (see *Scheme 4*).

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Experimental Part

General. MPLC: *Labomatic Laboprep-MPLC* unit *MD-50/80/100*. Flash chromatography (FC): silica gel *Si 60* (40–63 μ; *Merck*). TLC: *Merck* precoated plates silica gel *60* F_{254}, detection by 5% molybdophosphoric acid in EtOH (*Aldrich Chemicals Ltd*). M.p.: *Reichert* thermomicroscope. Optical rotation: *Jasco P-1020* polarimeter. IR: *Bruker IFS-48*; in cm^{-1} NMR[1]). *Bruker Avance-360*, *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. *Hyatellaquinone. (11*R*)/(11*S*)-11-(2′,3′,5′,6′-Tetramethoxyphenyl)drim-8(12)-en-11-ol* (=*(*α*R,1*R*,4a*R*,8-a*R*)/(*α*S,1*R*,4a*R*,8a*R*)-Decahydro-5,5,8a-trimethyl-2-methylene-α-(2,3,5,6-tetramethoxyphenyl)naphthalene-1-methanol*; **4a**,**b**). A mixture of 0.96 g (4.9 mmol) of dried 1,2,4,5-tetramethoxybenzene and 0.81 ml (5.3 mmol) of tetramethylethylenediamine in 60 ml of abs. THF is cooled to −78°, and 2.67 ml (5.34 mmol) of 2M BuLi in hexane is slowly added. After 30 min, a soln. of 0.73 g (3.3 mmol) of (+)-albicanal ((+)-**3**) in 25 ml of THF is added. Thirty minutes later, 1 ml of sat. NH_4Cl soln. is added, and the solvent is evaporated. The residue is dissolved in MeOH/H_2O 80:20 and the mixture filtered. Further purification is carried out by MPLC (*RP-8* column, MeOH/H_2O 80:20): 1.17 g (85%) of **4a**,**b**. White solid. TLC (hexane/AcOEt 7:1): R_f 0.21. As the product consists of two diastereoisomers, no further spectroscopic characterization was carried out.

(+)-11-(2′,3′,5′,6′-Tetramethoxyphenyl)drim-8(12)-ene (=*(4a*R*,5*R*,8a*R*)-Decahydro-1,1,4a-trimethyl-6-methylene-5-[(2,3,5,6-tetramethoxyphenyl)methyl]naphthalene*; (+)-**6**). A soln. of 0.40 g (0.96 mmol) of **4a**,**b** in 25 ml of dry THF is dropwise added to a stirred soln. of 0.16 g (23 mmol) of Li in liquid ammonia at −78°. The mixture is stirred for 15 min at −78°, 1.5 g of solid NH_4Cl is added, NH_3 is allowed to evaporate, and AcOEt is added. After addition of sat. NH_4Cl soln. and stirring for 20 min, the org. layer is separated, washed with brine, and filtered through silica gel. Further purification by MPLC (hexane/AcOEt 9:1) gives 0.31 g (80%) of (+)-**6**. White solid. TLC (hexane/AcOEt 4:1): R_f 0.60. $[\alpha]_D^{24} = +34$ ($c = 1.0$, $CHCl_3$). IR: 2930*s*, 2860*m*, 2850*m*, 1645*w*, 1590*m*, 1485*s*, 1460*s*, 1440*m*, 1425*m*, 1380*w*, 1360*w*, 1340*m*, 1240*s*, 1215*s*, 1180*w*, 1125*w*, 1085*s*, 1075*s*, 1060*s*, 1010*m*. ^{1}H- and ^{13}C-NMR: *Table 1*. MS: 402 ($M^{+\bullet}$, 84), 387 (5), 370 (65), 355 (31), 340 (5), 246 (11), 233 (32), 211 (100), 196 (81), 181 (29), 153 (15), 137 (15), 109 (12), 95 (17), 81 (12), 69 (20), 55 (15), 41 (15).

Ammonium Cerium Nitrate Solution. To a soln. of 4.3 ml of 1.19M $Ce(NH_4)_2(NO_3)_6$ in H_2O, 21 ml of H_2O and 25 ml of MeCN are added (*ca*. 0.1 mol $Ce(NH_4)_2(NO_3)_6$/l).

(+)-3-(Drim-8′(12′)-en-11′-yl)-2,5-dimethoxy-1,4-benzoquinone (=*3-[[(1*R*,4a*R*,8a*R*)-Decahydro-5,5,8a-trimethyl-2-methylenenaphthalen-1-yl]methyl]-2,5-dimethoxycyclohexa-2,5-diene-1,4-dione*; (+)-**7**) *and (+)-3-(Drim-8′(12′)-en-11′-yl)-4,5-dimethoxy-1,2-benzoquinone* (=*3-[[(1*R*,4a*R*,8a*R*)-Decahydro-5,5,8a-trimethyl-2-methylenenaphthalen-1-yl]methyl]-4,5-dimethoxycyclohexa-3,5-diene-1,2-dione*; (+)-**8**). To a soln. of (+)-**6** (0.41 g, 1.02 mmol) in 100 ml of MeCN/DMF 1:1, a soln. of $Ce(NH_4)_2(NO_3)_6$ (50.3 ml, 5.10 mmol) is slowly added at r.t. The mixture is stirred for 30 min, 100 ml of H_2O is added, and the mixture is diluted with Et_2O. The org. layer is washed with H_2O and brine, dried (Na_2SO_4), and evaporated. Further purification by FC (hexane/AcOEt 2:1) leads to 92 mg (24%) of (+)-**7** and 131 mg (34%) of (+)-**8**.

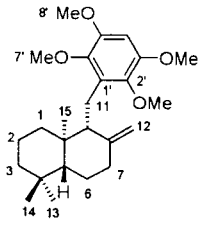
*Data of (+)-***7**: Yellow solid. TLC (hexane/AcOEt 7:3): R_f 0.24. M.p. 62°. $[\alpha]_D^{24} = +40$ ($c = 0.5$, $CHCl_3$). IR: 3022*m*, 2917*w*, 2252v*w*, 1650v*w*, 1596v*w*, 1224*w*, 1203*w*, 905*s*, 726*s*, 668*m*, 645*w*. ^{1}H- and ^{13}C-NMR: *Table 1*. MS: 372 (100, $M^{+\bullet}$), 357 (20), 340 (39), 255 (20), 241 (21), 216 (33), 203 (32), 189 (41), 182 (29), 69 (26). HR-MS: 372.2301 ($C_{23}H_{32}O_4^+$; calc. 372.2301).

*Data of (+)-***8**: TLC (hexane/AcOEt 1:1): R_f 0.43. $[\alpha]_D^{25} = +103$ ($c = 1.0$, $CHCl_3$). M.p. 122°. ^{1}H- and ^{13}C-NMR: *Table 1*. IR: 3025*m*, 3015*m*, 2972*m*, 1652*w*, 1580*w*, 1365*m*, 1260*w*, 1228*w*, 905*s*, 725*s*, 651*m*. MS: 372 (92, $M^{+\bullet}$), 190 (17), 189 (100), 182 (78), 167 (20), 154 (17), 153 (20), 119 (14), 69 (21), 41 (14). HR-MS: 372.2301 ($C_{23}H_{32}O_4^+$; calc. 372.2301).

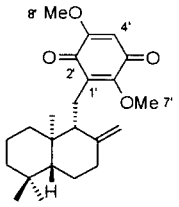
(+)-Hyatellaquinone (=*3-[[(1*R*,4a*R*,8a*R*)-Decahydro-5,5,8a-trimethyl-2-methylenenaphthalen-1-yl]methyl]-2-hydroxy-5-methoxycyclohexa-2,5-diene-1,4-dione*; **1**). A soln. of 44 mg (0.118 mmol) of (+)-**8** in 50 ml of MeCN is treated with 15 ml of 10% $HClO_4$ in H_2O. Within 15–20 min, the color of the soln. is changing from orange red to light yellow. To this mixture, 50 ml of H_2O and 40 ml of Et_2O are added. The org. layer is washed with H_2O and brine, dried (Na_2SO_4), and evaporated. The residue is purified by chromatography (silica gel, AcOEt): 42 mg (99%) of **1**. Yellow solid. M.p. 145°. TLC (hexane/AcOEt 1:1): R_f 0.80. $[\alpha]_D^{24} = +15$ ($c = 0.5$, $CHCl_3$) ([1]: $[\alpha]_D^{24} = +15.6$ ($c = 0.5$, $CHCl_3$). IR: 3390 (br.), 3022*m*, 2927*w*, 2360*w*, 1652*m*, 1647*m*, 1615*m*, 1264*w*, 1227*m*, 1204*w*, 674*w*. ^{1}H- and ^{13}C-NMR: *Table 1*. MS: 358 (44, $M^{+\bullet}$), 207 (17), 190 (17), 189 (100), 169 (23), 168 (49), 137 (17), 95 (17), 69 (20), 41 (12). HR-MS: 358.2144 ($C_{22}H_{30}O_4^+$; calc. 358.2144).

2. *Spongiaquinone. (±)-Drimanic Acid Methyl Ester* (=*(1*RS*,2*RS*,4a*RS*,8a*RS*)-Decahydro-2,5,5,8a-tetramethylnaphthalene-1-carboxylic Acid Methyl Ester*; (±)-**11**). A soln. of 2.95 g (11.8 mmol) of (±)-albicanic acid methyl ester ((±)-**9**) and 257 mg (0.72 mmol) of $[RhCl(Ph_3P)_3]$ in 60 ml of benzene and 30 ml of MeOH is

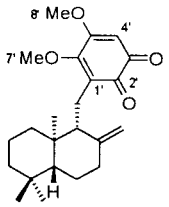
Table 1. *^{1}H- and ^{13}C-NMR Data of Compounds (+)-**6**, (+)-**7**, (+)-**8**, and **1***[1]). Coupling constants *J* in Hz.



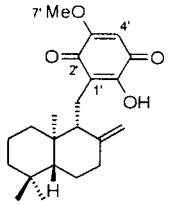
(+)-**6**



(+)-**7**



(+)-**8**



1

	(+)-**6**[a])		(+)-**7**[b])		(+)-**8**[b])		**1**[b])	
	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)
CH_2(1)	38.5	1.29 1.85	38.7	1.39 1.78	38.7	1.36 1.75	38.8	1.36 1.76
CH_2(2)	19.6	1.49 1.59	19.2	1.52 1.57	19.4	1.52 1.57	19.4	1.51 1.57
CH_2(3)	42.2	1.18 1.37	42.2	1.22 1.40	42.1	1.21 1.38	42.1	1.19 1.37
C(4)	33.6	–	33.3	–	33.6	–	33.6	–
H–C(5)	55.5	1.17	55.6	1.15	55.5	1.12	55.5	1.14
CH_2(6)	24.5	1.31 1.66	24.5	1.31 1.70	24.4	1.29 1.69	24.5	1.28 1.68
CH_2(7)	38.5	1.89 2.23	38.4	1.91 2.29	38.3	1.90 2.27	38.4	1.90 2.28
C(8)	148.8	–	148.9	–	148.6	–	148.8	–
H–C(9)	55.7	2.55	55.0	2.26	54.7	2.27	54.2	2.35
C(10)	40.1	–	40.2	–	40.1	–	40.1	–
CH_2(11)	20.1	2.72 (*dd*, *J* = 13.4, 2.9), 2.77 (*dd*, *J* = 13.4, 10.1)	19.5	2.47 (*dd*, *J* = 13.6, 2.9), 2.67 (*dd*, *J* = 13.6, 10.7)	19.5	2.47 (*dd*, *J* = 13.8, 2.9), 2.60 (*dd*, *J* = 13.8, 10.8)	18.8	2.51 (*dd*, *J* = 14.0, 3.0), 2.62 (*dd*, *J* = 14.0, 10.8)
CH_2(12)	106.9	4.65, 5.00	106.7	4.64, 4.66	106.9	4.62, 4.65	106.5	4.65 (*s*), 4.67 (*s*)
Me(13)	33.6	0.84 (*s*)	33.6	0.84 (*s*)	33.5	0.84 (*s*)	33.6	0.84 (*s*)
Me(14)	21.7	0.80 (*s*)	21.7	0.79 (*s*)	21.6	0.78 (*s*)	21.7	0.79 (*s*)
Me(15)	14.1	0.80 (*s*)	14.1	0.74 (*s*)	14.1	0.72 (*s*)	14.0	0.74 (*s*)
C(1′)	130.6	–	130.9	–	131.4	–	119.4	–
C(2′)	141.2	–	182.8	–	178.8	–	182.0	–
C(3′)	148.7	–	158.8	–	181.0	–	161.2	–
H–C(4′)	96.3	6.37 (*s*)	105.3	5.67 (*s*)	101.3	5.63 (*s*)	102.1	5.78 (*s*)
C(5′)	148.7	–	183.3	–	166.3	–	182.5	–
C(6′)	141.2	–	156.1	–	158.8	–	151.5	–
Me(7′)	60.7	3.73 (*s*)	61.2	4.04 (*s*)	56.7	3.85 (*s*)	56.7	3.81 (*s*)
Me(8′)	56.0	3.80 (*s*)	56.4	3.76 (*s*)	61.8	3.87 (*s*)	–	–
Me(9′)	56.0	3.80 (*s*)	–	–	–	–	–	–
Me(10′)	60.7	3.73 (*s*)	–	–	–	–	–	–
OH	–	–	–	–	–	–	–	7.39 (br. *s*)

[a]) *DRX-500* spectrometer. [b]) *Avance-360* spectrometer.

stirred at r.t. for 4 h under H_2 at 1 atm. After evaporation, the residue is dissolved in petroleum ether, the soln. filtrated through silica gel, and the solvent evaporated: 2.20 g (84%) of (±)-**11**. Colorless oil. TLC (hexane/AcOEt 17:1): R_f 0.45. IR: 2930*s*, 2870*m*, 2850*m*, 1725*s*, 1460*w*, 1435*w*, 1390*w*, 1265*w*, 1205*m*, 1190*m*, 1175*m*, 1150*m*, 1110*w*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.90 (H–C(1)); 1.60 (H–C(1)); 1.31 (H–C(2)); 1.38 (H–C(2));

1.11 (H–C(3)); 1.33 (H–C(3)); 0.74 (H–C(5)); 1.40 (H–C(6)); 1.43 (H–C(6)); 1.55 (H–C(7)); 1.59 (H–C(7)); 2.17 (H–C(8)); 2.20 (H–C(9)); 1.01 (*d*, *J* = 7.3, Me(12)); 0.80 (*s*, Me(13)); 0.78 (*s*, Me(14)); 1.18 (*s*, Me(15)); 3.56 (*s*, MeO). ^{13}C-NMR (125 MHz, $CDCl_3$): 39.5 (C(1)); 18.1 (C(2)); 42.0 (C(3)); 33.1 (C(4)); 55.9 (C(5)); 17.2 (C(6)); 33.9 (C(7)); 31.4 (C(8)); 59.3 (C(9)); 37.3 (C(10)); 174.3 (C(11)); 17.1 (Me(12)); 33.3 (Me(13)); 21.5 (Me(14)); 16.1 (Me(15)); 50.7 (MeO). MS: 252 (49, $M^{+\bullet}$), 237 (73), 221 (5), 205 (11), 196 (37), 177 (18), 163 (8), 137 (11), 123 (100), 109 (27), 101 (51), 95 (30), 81 (22), 69 (22), 55 (14). HR-MS: 252.2089 ($C_{16}H_{28}O_2^+$; calc. 252.2089).

(±)-11-(2′,3′,5′,6′-Tetramethoxyphenyl)driman-11-one (=*[(1*RS,*2*RS,*4a*RS,*8a*RS*)-Decahydro-2,5,5,8a-tetramethylnaphthalen-1-yl](2,3,5,6-tetramethoxyphenyl)methanone*; (±)-**12**). To a mixture of 1.37 g (6.91 mmol) of dry 1,2,4,5-tetramethoxybenzene and 1.14 ml (7.61 mmol) of tetramethylethylenediamine in 25 ml of dry THF, 3.04 ml (7.61 mmol) of 2M BuLi in hexane is dropwise added at 0°. After stirring for 30 min, a soln. of 0.92 g (3.45 mmol) of (±)-drimanic acid methyl ester ((±)-**11**) in 40 ml of dry THF is added. The mixture is stirred at 0° for 1 h. Then 2 ml of sat. NH_4Cl soln. is added. The org. layer is dried (Na_2SO_4) and adsorbed on silica gel. FC (silica gel; hexane/AcOEt 4:1) gives 0.48 g (33%) of (±)-**12** and 0.50 g (57%) of educt (±)-**11**. (±)-**12**: Light yellow oil. TLC (hexane/AcOEt 1:1): R_f 0.54. IR: 3020*s*, 2938*m*, 2848*w*, 2400v*w*, 2252v*w*, 1697*m*, 1590v*w*, 1482*m*, 1252*m*, 908*s*. ^{1}H- and ^{13}C-NMR: *Table 2*. MS: 418 (17, $M^{+\bullet}$), 267 (4), 226 (8), 225 (100), 210 (7),196 (6). HR-MS: 418.2719 ($C_{25}H_{38}O_5^+$; calc. 418.2719).

*(±)-(11*R*)/(11*S*)-11-(2′,3′,5′,6′-Tetramethoxyphenyl)driman-11-ol* (=*(α*RS,*1*RS,*2*RS,*4a*RS,*8a*RS*)/(α*RS,*1*SR,*2*SR,*4a*SR,*8a*SR*)-Decahydro-2,5,5,8a-tetramethyl-α-(2,3,5,6-tetramethoxyphenyl)naphthalene-1-methanol*; (±)-**5a**,**b**) *by Reduction of (±)-***12**. Ketone (±)-**12** (0.37 g, 0.88 mmol) is dissolved in 50 ml of dry CH_2Cl_2. The mixture is cooled to 0°, and 4.42 ml (4.42 mmol) of 1M diisobutylaluminium hydride (DIBAL) in CH_2Cl_2 is added. After stirring for 20 min, the soln. is poured into a mixture of 15 g of ice and 5 ml of conc. HCl soln. and stirred for additional 5 min. The aq. layer is extracted with AcOEt, and the combined org. layers are filtered through Na_2SO_4 and silica gel. The filtrate is evaporated and the residue purified by FC (silica gel, hexane/AcOEt 4:1): 0.35 g (95%) of (±)-**5a**,**b**. Colorless resin. TLC (hexane/Me_2CO 4:1): R_f 0.36. MS: 420 (3, $M^{+\bullet}$), 228 (11), 227 (100), 212 (15), 197 (8). HR-MS: 420.2876 ($C_{25}H_{40}O_5^+$; calc. 420.2876).

*(11*R*)/(11*S*)-11-(2′,3′,5′,6′-Tetramethoxyphenyl)drim-8(12)-en-11-ol* (=*(α*R,*1*S,*4a*S,*8a*S*)/(α*S,*1*S,*4a*S,*8a*S*)-Decahydro-5,5,8a-trimethyl-2-methylene-α-(2,3,5,6-tetramethoxyphenyl)naphthalene-1-methanol*; **13a**,**b**). As described for **4a**,**b**, with (–)-albicanal ((–)-**3**).

*(8*S,*11*R*)/(8*S,*11*S*)-11-(2′,3′,5′,6′-Tetramethoxyphenyl)driman-11-ol* (=*(α*R,*1*S,*2*S,*4a*S,*8a*S*)/(α*S,*1*S,*2*S,*4a*S,*8a* S*)-Decahydro-2,5,5,8a-tetramethyl-α-(2,3,5,6-tetramethoxyphenyl)naphthalene-1-methanol*; **5a**,**b**) *by Hydrogenation of* **13a**,**b**. To a soln. of 1.35 g (3.23 mmol) of **13a**,**b** in 100 ml of MeOH and 40 ml of AcOEt, 0.50 g of 10% Pd/C is added. The reaction vessel is evacuated and then filled with N_2. This procedure is repeated once. The mixture is stirred for 2 h under H_2 (detection of turnover by reversed-phase TLC). After filtration through silica gel, the solvent is evaporated: 1.27 g (94%) of **5a**,**b**. Colorless resin. Data of **5a**,**b**: see above.

(±)-11-(2′,3′,5′,6′-Tetramethoxyphenyl)drim-9(11)-ene (=*(2*RS,*4a*RS,*8a*RS*)-Decahydro-2,5,5,8a-tetramethyl-1-[(2,3,5,6-tetramethoxyphenyl)methylene]naphthalene*; (±)-**14**) *and (±)-(1*R,*2*S*)/(1*S,*2*R*)-1,2,3,4,5,6,7,8-Octahydro-1,2,5,5-tetramethyl-1-[(2,3,5,6-tetramethoxyphenyl)methyl]-naphthalene* ((±)-**15**). A soln. of 0.44 g (1.04 mmol) of (±)-**5a**,**b** in 15 ml of benzene is dropwise added to a mixture of 5 mg of $TsOH \cdot H_2O$ and 0.6 ml (2.92 mmol) of 1,1,1-trichloro-3,3,3-trifluoropropan-2-one in 15 ml of benzene. After heating under reflux for 1 h and cooling to r.t., 40 ml of Et_2O and 40 ml of sat. Na_2CO_3 soln. are added. The org. layer is separated and filtered through Na_2SO_4. The filtrate is evaporated and the residue purified by FC (silica gel, hexane/Me_2CO 15:1): 0.13 g (30%) of (±)-**14** and 0.16 g (38%) of (±)-**15** as colorless solids.

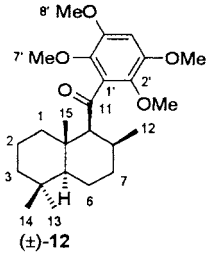
Data of (±)-**14**: TLC (hexane/Me_2CO 4:1): R_f 0.60. IR: 3427 (br.), 3018*s*, 2968*w*, 2914*w*, 2846*w*, 2398*w*, 2360*w*, 2330*w*, 1654*w*, 1261*w*, 1222*m*, 1204*m*, 1095*w*, 1041*w*, 669*s*. ^{1}H- and ^{13}C-NMR: *Table 2*. MS: 402 (100, $M^{+\bullet}$), 264 (25), 211 (14), 95 (8). HR-MS: 402.2770 ($C_{25}H_{38}O_4^+$; calc. 402.2770).

Data of (±)-**15**: TLC (hexane/Me_2CO 4:1): R_f 0.70. IR: 3103*s*, 2973*w*, 2918*w*, 2844*w*, 2396*w*, 2360*w*, 2336*w*, 1226*m*, 1200*m*, 1034*w*, 663*m*. ^{1}H- and ^{13}C-NMR: *Table 2*. MS: 402 (14, $M^{+\bullet}$), 233 (64), 212 (62), 191 (100), 135 (8). HR-MS: 402.2770 ($C_{25}H_{38}O_4^+$; calc. 402.2770).

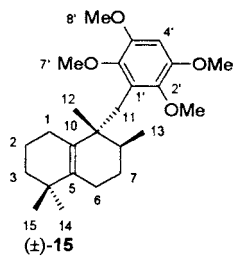
Ammonium Cerium Nitrate Solution. An 1.19M aq. soln. of $Ce(NH_4)_2(NO_3)_6$ (1.15 ml) is mixed with 5 ml of H_2O and 5 ml of MeCN.

(±)-3-(Drim-9′(11′)-enyl)-2,5-dimethoxy-1,4-benzoquinone (=*2,4-Dimethoxy-3-[(2*RS,*4a*RS,*8a*RS*)-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H*)-ylidene)methyl]cyclohexa-2,5-diene-1,4-dione*; (±)-**16**) *and (±)-Spongiaquinone* (=*2-Hydroxy-4-methoxy-3-{[(2*RS,*4a*RS,*8a*RS*)-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H*)-ylidene]methyl}cyclohexa-2,5-diene-1,4-dione*; (±)-**2**). To a soln. of 0.11 g (0.27 mmol) of (±)-**14** in 75 ml of MeCN/DMF 2:1, 11.2 ml of $Ce(NH_4)_2(NO_3)_6$ soln. (1.37 mmol) is dropwise added. After

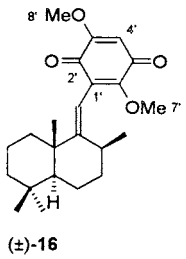
Table 2. *^{1}H- and ^{13}C-NMR Data of Compounds of (±)-***12**, *(±)-***14**, *(±)-***15**, *(±)-***16**, *and (±)-***2**[1]). Coupling constants *J* in Hz.



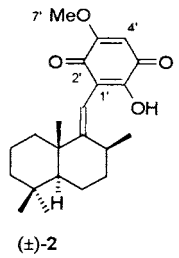
(±)-**12**



(±)-**15**



(±)-**16**



(±)-**2**

	(±)-**12**[a])		(±)-**14**[b])		(±)-**15**[a])		(±)-**16**[b])		(±)-**2**[b])	
	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)
CH_2(1)	38.4	1.17 1.99	38.9	1.51 1.68	25.8	1.38 2.05	38.5	1.41 1.82	38.5	1.48 1.79
CH_2(2)	18.3	1.37 1.67	18.9	1.53 1.70	20.1	1.61 (2 H)	18.7	1.53 1.67	18.9	1.51 1.67
CH_2(3)	42.2	1.14 1.33	42.1	1.17 1.39	40.1	1.37 1.43	41.9	1.14 1.38	41.9	1.18 1.36
C(4)	33.2	–	33.9	–	32.9	–	33.9	–	34.0	–
H–C(5) or C(5)	56.0	0.79	54.9	0.97	134.0	–	54.3	0.95	54.4	1.02
CH_2(6)	17.5	1.45 (2 H)	17.8	1.53 1.56	26.3	1.89 2.12	17.6	1.53 (2 H)	17.6	1.55 (2 H)
CH_2(7)	34.5	1.46 1.58	33.9	1.33 1.52	20.6	1.87 2.01	33.6	1.53 (2 H)	33.7	1.55 (2 H)
H–C(8)	30.0	2.25	32.2	2.74	33.1	1.80	32.8	2.48	33.4	2.52
H–C(9) or C(9)	67.1	2.80 (*d*, *J* = 3.92)	158.1	–	44.4	–	161.7	–	163.1	–
C(10)	29.7	–	40.9	–	132.4	–	41.1	–	41.3	–
C(11), H–C(11), or CH_2(11)	206.0	–	110.2	5.91 (*s*)	32.9	2.64 (*d*, *J* = 12.8), 2.77 (*d*, *J* = 12.8)	108.8	5.64 (*s*)	106.9	5.53 (*s*)
Me(12)	17.2	1.05 (*d*, *J* = 7.4)	21.3	1.06 (*d*, *J* = 7.5)	20.2	0.74 (*s*)	21.5	1.03 (*d*, *J* = 7.5)	21.9	1.08 (*d*, *J* = 7.5)
Me(13)	33.6	0.80 (*s*)	33.4	0.87 (*s*)	15.1	0.68 (*d*, *J* = 6.9)	33.3	0.85 (*s*)	33.5	0.86 (*s*)
Me(14)	21.8	0.82 (*s*)	21.8	0.87 (*s*)	28.9	0.95 (*s*)	21.8	0.85 (*s*)	21.9	0.87 (*s*)
Me(15)	17.5	1.33 (*s*)	22.4	1.19 (*s*)	27.8	1.02 (*s*)	22.3	1.16 (*s*)	22.4	1.17 (*s*)
C(1′)	149.0	–	128.9	–	128.3	–	124.0	–	125.5	–
C(2′)	133.3	–	140.2	–	142.2	–	182.3	–	181.3	–
C(3′)	138.6	–	148.7	–	148.6	–	159.0	–	161.3	–
H–C(4′)	98.7	6.49 (*s*)	96.5	6.42 (*s*)	96.7	6.42 (*s*)	105.2	5.78 (*s*)	102.3	5.84 (*s*)
C(5′)	138.6	–	148.7	–	148.6	–	183.2	–	182.7	–
C(6′)	133.3	–	140.2	–	142.2	–	154.5	–	150.2	–
Me(7′)	62.1	3.71 (*s*)	60.5	3.62 (*s*)	60.1	3.70 (*s*)	61.0	3.95 (*s*)	56.8	3.84 (*s*)
Me(8′)	56.3	3.83 (*s*)	56.2	3.83 (*s*)	55.9	3.83 (*s*)	56.4	3.79 (*s*)	–	–
Me(9′)	56.3	3.83 (*s*)	56.2	3.83 (*s*)	55.9	3.83 (*s*)	–	–	–	–
Me(10′)	62.1	3.71 (*s*)	60.5	3.62 (*s*)	60.1	3.70 (*s*)	–	–	–	–
OH	–	–	–	–	–	–	–	–	–	7.28 (br. *s*)

a) *Avance-360* spectrometer. [b]) *DRX-500* spectrometer.

disappearance of (±)-**14** (TLC control), 15 ml of 10% $HClO_4$ soln. is added, and the soln. is stirred for 15 min. To the mixture, 100 ml of H_2O and 50 ml of Et_2O are added, the org. layer is washed with H_2O and brine, dried (Na_2SO_4), and evaporated, and the residue purified by FC (hexane/AcOEt 4:1): 30 mg (30%) of (±)-**16** and 4 mg (4%) of (±)-**2**.

*Data of (±)-***16**: Yellow oil. TLC (hexane/AcOEt 1:1): R_f 0.87. IR: 3019*s*, 2967*w*, 2916*w*, 2852*w*, 2403*w*, 2361*m*, 2335*w*, 2254*w*, 1652*m*, 1263*w*, 1228*m*, 1205*m*, 908*s*, 665*s*. ^{1}H- and ^{13}C-NMR: *Table 2*. MS: 373 (46), 372 (100, $M^{+\bullet}$), 290 (13), 275 (11), 234 (75), 222 (57), 220 (54), 202 (15), 189 (17), 69 (14). HR-MS: 372.2300 ($C_{23}H_{32}O_4^+$; calc. 372.2301).

*Data of (±)-***2**: Red solid. TLC (hexane/AcOEt 1:1): R_f 0.44. IR: 3687*w*, 3616*w*, 3017*s*, 2976*w*, 2916*w*, 2848*w*, 2401*w*, 2361*w*, 2335*w*, 1653*w*, 1521*w*, 1227*m*, 1205*m*, 1046*w*, 930*w*, 669*m*. ^{1}H- and ^{13}C-NMR: *Table 2*. MS: 359 (32), 358 (100, $M^{+\bullet}$), 342 (93), 220 (71), 208 (53), 207 (74), 191 (21), 168 (31), 69 (21). HR-MS: 358.2144 ($C_{22}H_{30}O_4^+$; calc. 358.2144).

*(8*S*,11*R*)/(8*S*,11*S*)-11-(2′,3′,5′,6′-Tetramethoxyphenyl)driman-11-ol Acetate* (=*(α*R*,1*S*,2*S*,4a*S*,8a*S*)/(α*S*,1*S*,2*S*,4a*S*,8a*S*)-Decahydro-2,5,5,8a-tetramethyl-α-(2,3,5,6-tetramethoxyphenyl)naphthalene-1-methanol Acetate*; **17a**,**b**). To a soln. of 0.70 g (1.66 mmol) of **5a**,**b** and 41 mg (0.33 mmol) of DMAP in 15 ml of dry pyridine, 1.60 ml (16.60 mmol) of Ac_2O is added, and the mixture is heated for 4 h under reflux. The cold mixture is slowly poured into a AcOEt/ice/sat. aq. NaCl soln. 1:1:1 (*ca.* 60 ml). The aq. layer is extracted twice with AcOEt and the combined org. phase washed with 0.5M HCl, sat. $NaHCO_3$ soln., and brine, filtered through Na_2SO_4, and evaporated. FC (hexane/AcOEt 3:1) gives 0.60 g (78%) of **17a**,**b**. Colorless glue-like solid. TLC (hexane/Me_2CO 4:1): R_f 0.42. MS: 462 (55, $M^{+\bullet}$), 227 (100), 43 (37), 212 (11). HR-MS: 462.2981 ($C_{27}H_{42}O_6^+$; calc. 462.2981).

Ammonium Cerium Nitrate Solution. To 1.3 ml of 1.19M $Ce(NH_4)_2(NO_3)_6$ in H_2O, 7 ml of H_2O and 7 ml of MeCN are added (*ca.* 0.1M $Ce(NH_4)_2(NO_3)_6$/l).

*(8′*S*,11′*R*)/(8′*S*,11′*S*)-3-(11′-Acetoxydriman-11′-yl)-2,5-dimethoxy-1,4-benzoquinone* (=*3-{(1*R*)/(1*S*)-(Acetyloxy)[(1*S*,2*S*,4a*S*,8a*S*)-decahydro-2,5,5,8a-tetramethylnaphthalen-1-yl]methyl}-2,5-dimethoxycyclohexa-2,4-diene-1,4-dione*; **18a**,**b**) *and (8′*S*,11′*R*)/(8′*S*,11′*S*)-3-(11′-Acetoxydriman-11′-yl)-4,5-dimethoxy-1,2-benzoquinone* (=*3-{(1*R*)/(1*S*)-(Acetyloxy)[(1*S*,2*S*,4a*S*,8a*S*)-decahydro-2,5,5,8a-tetramethylnaphthalen-1-yl]methyl}-4,5-dimethoxycyclohexa-3,5-diene-1,2-dione*; **19a**,**b**). To a soln. of 0.15 g (0.32 mmol) of **17a**,**b** in 30 ml of MeCN/DMF 2:1, 15.4 ml of $Ce(NH_4)_2(NO_3)_6$ soln. (1.62 mmol) is dropwise added, and the mixture is stirred for 15 min. After addition of 50 ml of H_2O and 50 ml of Et_2O, the org. layer is washed with H_2O and brine, dried (Na_2SO_4), and evaporated, and the residue purified by FC (hexane/AcOEt 3:1): 18 mg (5%) of **18a**,**b**, 70 mg (50%) of **19a**,**b**, and 5 mg (4%) of spongiaquinone (**2**).

Data of **18a**,**b**: Yellow oil. TLC (hexane/Me_2CO 4:1): R_f 0.31. MS: 432 (1, $M^{+\bullet}$), 372 (12), 240 (30), 221 (12), 123 (9), 198 (100), 69 (9). HR-MS: 432.2512 ($C_{25}H_{36}O_6^+$; calc. 432.2512).

Data of **19a**,**b**: Red solid. TLC (hexane/Me_2CO 4:1): R_f 0.22. MS: 432 (5, $M^{+\bullet}$), 372 (90), 234 (26), 212 (27), 210 (34), 198 (81), 170 (100), 168 (34), 69 (27), 43 (27). HR-MS: 432.2512 ($C_{25}H_{36}O_6^+$; calc. 432.2512).

Spongiaquinone (=*2-Hydroxy-4-methoxy-3-{[(2*S*,4a*S*,8a*S*)-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H*)-ylidene]methyl}cyclohexa-2,5-diene-1,4-dione*; **2**). *Method A: Demethylation of* **19a**,**b** *by Perchloric Acid*. To a soln. of 30 mg (0.07 mmol) of **19a**,**b** in 15 ml of MeCN, 10 ml of 10% $HClO_4$ soln. is added. The color of the soln. is changing from orange red to yellow. After stirring for 1 h, the mixture is diluted with 60 ml of brine/H_2O/Et_2O 1:1:1 and the org. layer filtered through Na_2SO_4. Further purification by FC (hexane/AcOEt 1:1) yields 12 mg (48%) of **2**. Red solid. Data of (±)-**2**, see above.

Method B: Demethylation of **19a**,**b** *by TsOH · H_2O.* A soln. of 26 mg (0.06 mmol) of **19a**,**b** and 24 mg (0.13 mmol) of $TsOH \cdot H_2O$ in 20 ml of dry benzene is stirred for 2 h at 35°. For purification, the mixture is adsorbed on silica gel and submitted to FC (hexane/AcOEt 1:1): 16 mg (74%) of **2**. Red solid. M.p. 158° ([3]: M.p. 159–160°). Data for (±)-**2**, see above.

Spongiaquinone Methyl Ether ((=*(2,4-Dimethoxy-3-{[(2*S*,4a*S*,8a*S*)-octahydro-2,5,5,8a-tetramethylnaphthalen-1(2*H*)-ylidene]methyl}cyclohexa-2,5-diene-1,4-dione*; (−)-**16**). To a mixture of 20 mg (0.06 mmol) of **2** in 20 ml of Me_2CO saturated with K_2CO_3, 0.03 ml (0.56 mmol) of MeI is added, and the mixture is stirred for 24 h at r.t. After addition of 1 ml of 1M NaOH in H_2O and stirring for 30 min, the mixture is adsorbed on silica gel and submitted to FC (hexane/AcOEt 1:1): 20 mg (95%) of (−)-**16**. Yellow oil. For optical-rotation measurements the compound is purified by MPLC (hexane/AcOEt 4:1) and dried under high vacuum. $[\alpha]_D^{23} = -82$ ($c = 1.0$, $CHCl_3$) ([2]: $[\alpha]_D = -82$ ($c = 0.5$, $CHCl_3$). Data for (±)-**16**, see above.

REFERENCES

[1] R. Talpir, A. Rudi, Y. Kashman, Y. Loya, A. Hizi, *Tetrahedron* **1994**, *50*, 4179.
[2] R. J. Capon, D. R. Groves, S. Urban, R. G. Watson, *Aust. J. Chem.* **1993**, *46*, 1245.
[3] R. Kazlauskas, P. T. Murphy, R. G. Warren, R. J. Wells, J. F. Blount, *Aust. J. Chem.* **1978**, *31*, 2685.
[4] S. Loya, R. Tal, Y. Kashman, A. Hizi, *Antimicrob. Agents Chemother.* **1990**, *34*, 2009.
[5] M.-L. Bourguet-Kondracki, A. Longeon, E. Morel, M. Guyot, *Int. Immunopharmac.* **1991**, *13*, 393.
[6] H. S. Radeke, C. A. Digits, S. D. Bruner, M. L. Snapper, *J. Org. Chem*. **1997**, *62*, 2823.
[7] J. C. Swersey, L. R. Barrows, C. M. Ireland, *Tetrahedron Lett*. **1991**, *32*, 6687.
[8] S. Poigny, T. Huor, M. Guyot, M. Samadi, *J. Org. Chem*. **1999**, *64*, 9318.
[9] D. Herlem, J. Kervagoret, D. Yu, F. Khuong-Huu, A. S. Kende, *Tetrahedron* **1993**, *49*, 607.
[10] M. Liapis, V. Ragoussis, N. Ragoussis, *J. Chem. Soc., Perkin Trans. 1* **1985**, 815.
[11] V. Ragoussis, M. Liapis, N. Ragoussis, *J. Chem. Soc., Perkin Trans. 1* **1987**, 987.
[12] T. Laube, J. Schröder, R. Stehle, K. Seifert, *Tetrahedron* **2002**, *58*, 4299.
[13] S. Poigny, M. Guyot, M. Samadi, *Tetrahedron* **1998**, *54*, 14791.
[14] R. J. Capon, in 'Studies in Natural Products Chemistry, Structure and Chemistry, Part C', Ed. Atta-ur-Rahman, Elsevier, Amsterdam, 1995, Vol. 15, p. 289.
[15] S. Abdel-Baky, A. Moussa, *Synth. Commun*. **1988**, *18*, 1795.

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