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Aporphinoid alkaloids and other constituents from *Lettowianthus stellatus*☆

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Abstract

Two new aporphinoid alkaloids, lettowianthine and 11-methoxylettowianthine were isolated from the root bark of *Lettowianthus stellatus*, together with the new sesquiterpene 11-hydroxyguaia-4,6-diene and the known compounds liriodenine, (*Z*)-7-octadecen-9-ynoic acid, methyl (2*E*,6*E*,10*R*)-10,11-epoxy-3,7,11-trimethyl-2,6-dodecadienoate, methyl (2*E*,6*E*,10*R*)-10,11-dihydroxy-3,7,11-trimethyl-2,6-dodecadienoate, and 3,4,5-trimethoxyphenol. The structure elucidation was achieved by spectroscopic methods. © 2000 Published by Elsevier Science Ltd. All rights reserved.

Keywords: *Lettowianthus stellatus*; Annonaceae; Aporphinoid alkaloids; Lettowianthine; 11-Methoxylettowianthine; 11-Hydroxyguaia-4,6-diene; (*Z*)-7-Octadecen-9-ynoic acid; Methyl (2*E*,6*E*,10*R*)-10,11-epoxy-3,7,11-trimethyl-2,6-dodecadienoate; Methyl (2*E*,6*E*,10*R*)-10,11-dihydroxy-3,7,11-trimethyl-2,6-dodecadienoate

1. Introduction

Plants of the family Annonaceae are known as a rich source of aporphinoid and other isoquinoline-type alkaloids (Guinaudeau, Leboeuf & Cavé, 1988; Leboeuf, Cavé, Bhaumik, Mukherjee & Mukherjee, 1982; Waterman, 1986). Furthermore, quite a number of non-alkaloidal natural products with unusual structural features and interesting biological activities have been isolated from species of this family (Leboeuf et al., 1982; Waterman, 1986).

In the course of our recent investigations of several *Uvaria* species, we isolated various novel compounds, among them benzylated dihydrochalcones (Achenbach, Höhn, Waibel, Nkunya, Jonker & Muhie, 1997) and other flavonoids (Nkunya, Waibel & Achenbach, 1993), oxygenated pyrenes (Achenbach et al., 1997) and benzopyranyl sesquiterpenes (Weenen, Nkunya, Mgani, Posthumus, Waibel & Achenbach, 1991). Some of the isolated compounds exhibited pronounced antimalarial activities (Nkunya, Weenen, Bray, Mgani & Mwasumbi, 1991).

We now report the results of a phytochemical analysis of the root bark of *Lettowianthus stellatus* Diels (Annonaceae), a plant growing in coastal rain forests of Kenya and Tanzania (Verdcourt, 1971). Root and stem barks of the plant are sold by herbal drug vendors in Dar es Salaam as remedies for stomach disorders and malaria related fevers.

We found extracts of the root bark to exhibit weak antimalarial activity in vitro against the multidrug resistant K1 strain and the chloroquine sensitive NF54 strain of *Plasmodium falciparum*. Our efforts to isolate the active constituent(s) yielded the hitherto unknown telisatin-type aporphinoids lettowianthine (**1**) and 11-

☆ Part 90 in the series 'Constituents of Tropical Medicinal Plants'. For Part 88, see Sung'hwa, Mgina, Jonker, Nkunya, Waibel and Achenbach (1999); for Part 89, see Asomaning et al. (1999).

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Table 1
^{1}H- and ^{13}C-NMR data on compounds **1**, **2** and **8** (δ in $CDCl_3$, J (Hz))

Position	**1**			**2**			**8**[a]		
	^{13}C		^{1}H	^{13}C[b]		^{1}H	^{13}C		^{1}H
1	143.1		–	143.5		–	146.6		–
1a	119.9		–	n.d.[c]		–	129.3		–
1b	112.8		–	113.4		–	112.2		–
2	151.5		–	151.8		–	157.1		–
3	109.2	7.12 *t*	1	109.2	7.11 *t*	1	112.3	7.18 *t*	1
3a	129.6		–	129.8		–	130.7		–
4	27.5	3.33 *dt*	1, 6.5	27.7	3.33 *dt*	1, 6.5	27.6	3.36 *dt*	1, 6.4
5	36.7	3.97 *t*	6.5	36.5	3.95 *t*	6.5	36.5	3.99 *t*	6.4
6a	153.7		–	153.8		–	153.3		–
7	103.1		–	102.8		–	103.2		–
7a	126.9		–	128.0		–	127.5		–
8	123.6	8.60 *br dd*	8, 1.5	115.8	8.23 *dd*	8, 1.5	123.7	8.65 *dd*	8.3, 1.8
9	128.3	7.64 *ddd*	8, 7, 1	130.5	7.59 *dd*	8, 8	129.2	7.65 *ddd*	8.3, 8.3, 1.8
10	125.3	7.50 *ddd*	8.5, 7, 1.5	107.9	7.00 *dd*	8, 1	125.6	7.52 *ddd*	8.3, 8.3, 1.8
11	127.6	8.85 *br dd*	8.5, 1	157.9		–	128.3	9.43 *dd*	8.3, 1.8
11a	124.5		–	114.1		–	125.8		–
C–C=O	179.9		–	n.d.[c]		–	180.0		–
N–C=O	160.3		–	n.d.[c]		–	160.3		–
OCH_2O	102.3	6.36 *s*		101.2	6.23 *s*		–		–
OMe	–		–	55.8	4.02 *s*		–		–

[a] Values reported by Menachery et al. (1995); further signals for two methoxy groups at δ 3.96 and δ 4.11 in the ^{1}H-NMR and at δ 56.6 and δ 60.0 in the ^{13}C-NMR, respectively.
[b] Values taken from HMQC and HMBC spectra with an uncertainty of ca. 0.3 ppm.
[c] n.d.: no correlations to these carbons were detected.

methyoxylettowianthine (**2**), the novel sesquiterpene 11-hydroxyguaia-4,6-diene (**3**), and the known compounds liriodenine (**4**), (*Z*)-7-octadecen-9-ynoic acid (**5**), methyl (2*E*,6*E*,10*R*)-10,11-epoxy-3,7,11-trimethyl-2,6-dodecadienoate (**6**), methyl (2*E*,6*E*,10*R*)-10,11-dihydroxy-3,7,11-trimethyl-2,6-dodecadienoate (**7**), and 3,4,5-trimethoxyphenol.

2. Results and discussion

Repeated chromatographic separation of the petrol, chloroform and ethanol extracts from the root bark of *L. stellatus* afforded the constituents **1**–**7** and 3,4,5-trimethoxyphenol. The intensively colored compounds **1**, **2** and **4**, which were isolated from the ethanol extract, exhibited the typical spectroscopic properties of aporphinoid alkaloids (Guinaudeau et al., 1988) and, subsequently, **4** was identified as liriodenine (**4**) by its physicochemical data and by comparison with an authentic sample (Achenbach & Löwel, 1995).

The ^{1}H-NMR spectrum (Table 1) of the dark red compound **1** ($C_{19}H_{11}NO_4$ by HRMS) indicated a dioxymethylene group (δ 6.36, 2H, *s*), four hydrogens at the aromatic ring D and a non-aromatic ring B as structural elements. The presence of two carbonyl groups followed from IR bands at 1748 and 1703 cm^{-1}, and from ^{13}C-NMR signals at δ 179.9 and 160.3, respectively. These data and information from heteronuclear correlation spectroscopy, particularly HMBC, established the partial structure shown in Fig. 1. No correlation signal was detected to the carbonyl carbon resonance appearing at δ 179.9, even in an experiment optimized on very small coupling constants. However, this carbonyl group had to be linked between C-7 and the amide carbon at N-6, due to the molecular formula, the significantly low field shift of H-8 and the UV/Vis spectrum, which demanded an extended chromophore.

Only a few aporphinoid alkaloids with the proposed molecular skeleton are known (Menachery, Blake, Gourley & Freyer, 1995; Roblot, Hocquemiller &

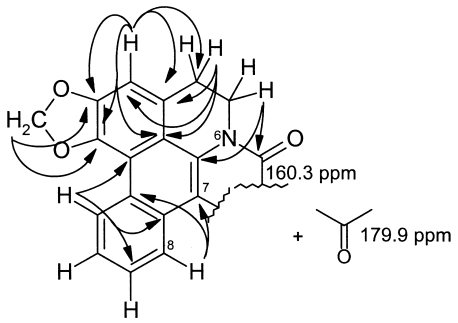


Fig. 1. Partial structure of **1** as established by HMBC. Important correlations are indicated by arrows.

Table 2
^{1}H- and ^{13}C-NMR data of compound **3** (δ in C_6D_6, J (Hz))

Position	^{13}C		^{1}H	H–C long range correlation to ^{13}C signal at:
1	54.1	2.49 *m*		–
		2.00 *dddd*	4.5, 8, 9, 12.5	36.9, 39.3, 54.1, 136.8, 137.1
2	30.1			
		1.43 *dddd*	7, 7, 9.5, 12.5	36.9, 39.3, 54.1, 136.8
		2.17 *ddd*	7, 8, 16	30.1, 136.8, 137.1
3	36.9			
		2.29 *br ddd*	4.5, 9.5, 16	136.8, 137.1
4	136.8[a]		–	–
5	137.1[a]		–	–
6	118.0	6.54 *br s*		26.6, 54.1, 73.7, 136.8, 137.1, 148.1
7	148.1		–	–
		2.02 *ddd*	2.5, 9, 16.5	36.2, 39.3, 73.7, 118.0, 148.1
8	26.6			
		2.42 *ddd*	2.5, 10, 16.5	36.2, 39.3, 73.7, 118.0, 148.1
		1.35 *dddd*	2.5, 7, 9, 14	21.7, 26.6, 39.3, 148.1
9	36.2			
		1.81 *dddd*	2.5, 5, 10, 14	21.7, 26.6, 39.3, 54.1, 148.1
10	39.3	1.53 *dqdd*	5, 6.5, 7, 11	21.7, 26.6, 30.1, 36.2, 54.1
11	73.7		–	–
12	29.0[a]	1.28 *s*		29.0 or 29.2, 73.7, 148.1
13	29.2[a]	1.28 *s*		29.0 or 29.2, 73.7, 148.1
14	14.7	1.72 *br s*		36.9, 136.8, 137.1
15	21.7	0.95 *d*	6.5	36.2, 39.3, 54.1

[a] Similar values might be interchanged.

Cavé, 1981; Lenz & Koszyk, 1984; Saá, Guitián, Castedo, Suau & Saá, 1986; Saá & Cava, 1978), most of them have been obtained as synthetic compounds (Lenz & Koszyk, 1984; Saá et al., 1986; Saá & Cava, 1978). Among the naturally occurring alkaloids of this group, the structurally most similar to **1** is telisatin A (**8**), a constituent of *Telitoxicum peruvianum* (Menispermaceae) (Menachery et al., 1995), whose structure has been established by comparison with a synthetic reference compound (Menachery et al., 1995; Saá et al., 1978). All basic spectroscopic properties described for **8** correlated well with those of alkaloid **1** isolated from *L. stellatus*. Compound **1** was named lettowianthine (**1**).

The similarity of the spectra of compound **2** and lettowianthine (**1**) indicated the same aporphinoid structures, and corresponding differences in the NMR spectra suggested for **2** an additional methoxy substituent at C-11. This was corroborated by NOE and HMBC experiments.

Compound **3** ($C_{15}H_{24}O$ by HRMS) exhibited the typical spectroscopic properties of a bicyclic sesquiterpene. The presence of four methyl groups, one of them bonded to an olefinic carbon (δ_H 1.72, δ_C 14.7), was indicated by the ^{1}H- and ^{13}C-NMR spectra (Table 2). Homonuclear COSY, HMQC and HMBC experiments enabled the assignment of all ^{1}H- and ^{13}C-NMR signals and established structure **3**. The relative configuration resulted from the detailed analysis of the ^{1}H-NMR data (Table 2) and from NOE studies (Fig. 2). The large constant observed for the coupling between H-1 and H-10 indicated the trans-orientation of these two protons.

A sesquiterpene with the same constitution but different stereochemistry, 11-hydroxyguaiene (**9**), has been reported from *Parthenium hysterophorus* (Asteraceae) (Bohlmann, Zdero & Lonitz, 1977). Recently, stereoselective synthesis of the (−)-enantiomer of **9** afforded a product with different physicochemical properties and suggested the revision of the structure originally claimed for **9** (Lee & Yoon, 1996).

The straight chain unsaturated fatty acid **5** ($C_{18}H_{30}O_2$ by HRMS) was isolated as the main component of the petrol extract. Its spectroscopic properties indicated a conjugated enyne system (ν_{max} 2210

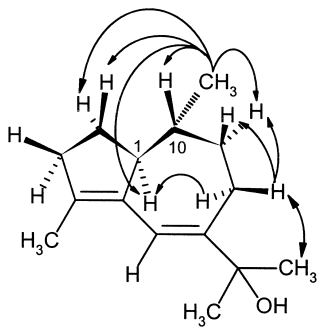


Fig. 2. Important NOEs observed for compound **3**.

cm^{-1}; λ_{max} 227 nm) with a *Z*-configurated double bond (δ_H 5.79, *dt*, J = 11, 7.5 Hz, δ_H 5.44, *br d*, J = 11 Hz). The position of the enyne moiety between C-7 and C-10 was deduced from COSY, relayed COSY, and TOCSY experiments. Relayed COSY correlations were observed from both the allylic protons H-6 (δ 2.30) and the protons H-2 (δ 2.36) to the methylene protons (H-4) the signal of which appeared as a multiplet at δ 1.39. The position of the double bond between C-7 and C-8 was further corroborated by the intense MS fragment at m/z 180 ($C_{11}H_{16}O_2$), which resulted from a 'retro diene cleavage' involving the triple bond at C-9/C-10.

According to the literature, the acid **5** was isolated only from *Paramacrolobium caeruleum* (Fabaceae) by Patil, Chan, Lois-Flamberg, Mayer & Westley (1989). The reported ^{1}H-NMR data completely agreed with those measured for **5**. However, discrepancies came up regarding the ^{13}C-NMR data. Obviously, the earlier authors have not been able to detect the signal of C-2, which in fact appeared with very low intensity; it was recognizable undoubtfully only in the HMQC and HMBC spectra.

The linear sesquiterpenes **6** and **7**, isolated from the petrol and chloroform extracts, were identified by comparison of their spectroscopic properties with literature data as methyl (2*E*,6*E*,10*R*)-10,11-epoxy-3,7,11-trimethyl-2,6-dodecadienoate (**6**) (Mori & Mori, 1987) and methyl (2*E*,6*E*,10*R*)-10,11-dihydroxy-3,7,11-trimethyl-2,6-dodecadienoate (**7**) (Mori & Mori, 1987), respectively.

The absolute configuration of **7** was corroborated applying Mosher's method (Dale & Mosher, 1973). Comparing the ^{1}H-NMR spectra of (*S*)- and (*R*)-MTPA-7; the resonances of H-6, H-8 and H-9 were found at lower field in the spectrum of (*S*)-MTPA-7; whereas in the spectrum of (*R*)-MTPA-7, the signals of the methyl groups bound to C-11 appeared at lower field. This established the *R*-configuration at C-10. Additionally, the ^{1}H-NMR spectra of the MTPA-esters of **7** revealed that the isolated compound was not enantiomerically pure but contained about 15% of *ent*-**7**.

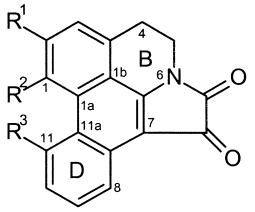
The (−)-enantiomer of the diol **7** has been reported from another Annonaceae species, *Cleistopholis patens* by Waterman and Muhammad (1985). Recently, compound **7** (or its enantiomer) was also isolated from *C. staudtii*, but no optical rotation was reported (Tane, Ayafor & Sondengam, 1988).

Compound **6** was established as enantiomerically pure by ^{1}H-NMR measurement in the presence of the chiral solvating reagent (*R*)-2,2,2-trifluoro-1-(9-anthryl)ethanol (Mori & Mori, 1987; Pirkle, Sikkenga & Pavlin, 1977).

The co-occurrence of **6** and **7**, and particularly the impurification of **7** with *ent*-**7**, suggested a potential artificial formation of the diol **7** from the epoxide **6** during work-up of the plant material. However, compound **6** proved stable under simulated extraction and chromatographic procedures. Nonetheless, a slow conversion of **6** into **7** was noticed upon prolonged storage of **6** in chloroform at about 8°C (refrigerator).

Compound **6**, known as insect juvenile hormone III, represents a common hormone of various insects, but it hitherto was isolated only once as a constituent of a higher plant (Toong, Schooley & Baker, 1988), where it might act as an insect defending agent.

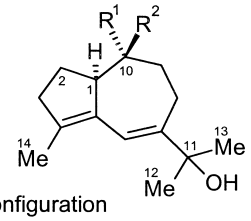
Compound **6** showed weak antimalarial activity in vitro against the multidrug resistant K1 strain and the chloroquine sensitive NF54 strain of *Plasmodium falciparum*. The other compounds were obtained in too small amounts for antimalarial assays.



1 $R^1 + R^2 = OCH_2O$, $R^3 = H$

2 $R^1 + R^2 = OCH_2O$, $R^3 = OMe$

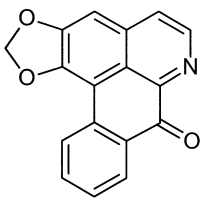
8 $R^1 = R^2 = OMe$, $R^3 = H$



rel. configuration

3 $R^1 = Me$, $R^2 = H$

9 $R^1 = H$, $R^2 = Me$



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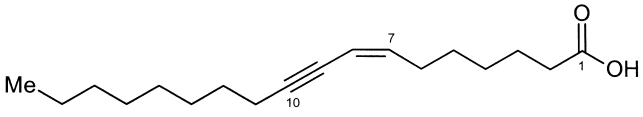

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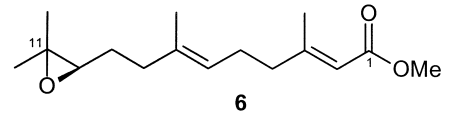

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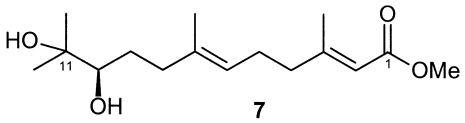

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3. Experimental

3.1. General

Mps uncorrected. TLC was performed on precoated plates (Silica gel 60 F_{254}, Merck) using CH_2Cl_2–Me_2CO (4:1) as the eluent; detection by UV and anisaldehyde reagent (Stahl & Kaltenbach, 1961). For CC silica gel 60 (Merck) or Sephadex® LH-20 (Pharmacia) were used. Vacuum liquid chromatography (VLC) was performed with silica gel 60 (Merck) eluting with *n*-hexane containing increasing amounts of EtOAc. HPLC on Eurospher RP-18, 7 μ (Knauer), with MeCN–H_2O (3:2) as the eluent. Unless otherwise stated, $[\alpha]_D$ at 21°C in $CDCl_3$, IR in KBr, UV in MeOH. If not otherwise stated, ^{1}H- and ^{13}C-NMR in $CDCl_3$ at 360 and 90 MHz, respectively; int. standard: TMS for ^{1}H, solvent for ^{13}C. EIMS at 70 eV using direct inlet; unless key ions only ions ≥20% and m/z >100 are presented. The antimalarial tests were carried out as previously described (Nkunya et al., 1991).

3.2. Plant material

Root bark of *L. stellatus* Diels was collected from the Udzungwa mountains (Kilombero district, Morogoro region) and from Zigi valley in East Usambara mountains (Tanga region) in July 1992 and December 1993. The plant was identified by Mr. L.B. Mwasumbi from the Herbarium of the Department of Botany, University of Dar es Salaam, where a voucher specimen is preserved under No. Mwasumbi 16383.

3.3. Extraction and isolation

Air dried and pulverised root bark (4 kg) was extracted at room temperature consecutively with petrol, $CHCl_3$ and EtOH for 2 days, and the concd extracts were fractionated by VLC. The petrol extract after VLC, CC on silica gel [*n*-hexane–EtOAc (4:1)], preparative TLC on RP-18 [MeOH–H_2O (9:1)] and subsequent CC on Sephadex® LH-20 [$CHCl_3$–MeOH (1:1)] afforded **5** (17 mg). Separation of the $CHCl_3$ extract by VLC and repeated CC on silica gel [*n*-hexane–EtOAc (4:1)] yielded **3** (33 mg) and **6** (48 mg). VLC of the EtOH extract gave three main fractions (E1–E3), which after repeated CC on silica gel [$CHCl_3$–MeOH (49:1)] and Sephadex® LH-20 [$CHCl_3$–MeOH (1:1)] yielded a further amount of **5** (42 mg, from E1), **4** (5.5 mg, from E2), **7** (43 mg, from E3), 3,4,5-trimethoxyphenol (15 mg, from E3) and a mixture of the aporphinoids **1** and **2** (from E3) which was subsequently separated by HPLC to give the pure compounds **1** (28 mg) and **2** (1 mg).

3.4. Lettowianthine (*1*)

Dark red solid. Mp 314–317°C, dec. (from $CHCl_3$). TLC: R_f 0.61. IR ν_{max} cm^{-1}: 3017, 2953, 2928, 1748, 1703, 1625, 1610, 1584, 1532. UV/Vis λ_{max} nm (log ε): 254 (4.02), 293 (3.42), 323 sh (3.50), 333 (3.55), 365 (3.23), 509 (3.07). ^{1}H-NMR: Table 1. ^{13}C-NMR: Table 1. MS m/z (rel. int.): 317.0692 $[M]^+$ (100) (calcd. for $C_{19}H_{11}NO_4$: 317.0688), 289.0736 (73) (calcd. for $C_{18}H_{11}NO_3$: 289.0734), 261.0796 (54) (calcd. for $C_{17}H_{11}NO_2$: 261.0790), 260 (31), 232 (21), 204 (25), 203 (40), 176 (20), 129 (20).

3.5. 11-Methoxylettowianthine (*2*)

Dark red amorphous solid. TLC: R_f 0.61. IR ν_{max} cm^{-1}: 3018, 2955, 2925, 1751, 1700. UV/Vis λ_{max} nm (log ε): 260 (4.09), 292 (3.48), 311 sh (3.28), 355 (3.25), 505 (3.02). ^{1}H-NMR: Table 1. ^{13}C-NMR: Table 1. MS m/z (rel. int.): 347.0792 $[M]^+$ (100) (calcd. for $C_{20}H_{13}NO_5$: 347.0794), 319 (80), 291 (28), 248 (52), 233 (21), 190 (20).

3.6. Liriodenine (*4*)

Yellow solid. Mp 280–281°C (from $CHCl_3$). TLC: R_f 0.07. Identical with an authentic sample (Achenbach & Löwel, 1995).

3.7. 11-Hydroxyguaia-4,6-diene (*3*)

Colorless oil. TLC: R_f 0.58; anisaldehyde: blue. $[\alpha]_D$ −55° (*c* 0.25). IR (film) ν_{max} cm^{-1}: 3400, 2969, 2952, 2927. UV λ_{max} nm: 248 (log ε 3.73). ^{1}H-NMR: (Table 2). ^{13}C-NMR: (Table 2). MS m/z (rel. int.): 220.1830 $[M]^+$ (36) (calcd. for $C_{15}H_{24}O$: 220.1827), 205.1594 (100) (calcd. for $C_{14}H_{21}O$: 205.1592), 177 (52), 159 (20), 145 (22), 121 (34), 119 (20), 105 (25), 43 (64).

3.8. (*Z*)-7-Octadecen-9-ynoic acid (*5*)

Colorless oil. TLC: R_f 0.48; anialdehyde: greenish grey. IR, UV, ^{1}H-NMR and MS identical with published data (Patil et al., 1989). ^{13}C-NMR: δ 14.1 (C-

18), 19.5 (C-11), 22.6 (C-17), 24.5 (C-3), 28.5–29.7 (C-4–C-6, C-12–C-15), 31.8 (C-16), 34.0 (C-2), 77.2 (C-9), 94.7 (C-10), 109.7 (C-8), 142.0 (C-7), 179.4 (C-1).

3.9. Methyl (2E,6E,10R)-10,11-epoxy-7,9,11-trimethyl-2,6-dodecadienoate (6)

Colorless oil. TLC: R_f 0.62; anisaldehyde: green. $[\alpha]_D$ +4.5° (*c* 0.7); (Mori & Mori, 1987): $[\alpha]_D$ +6.7° (*c* 0.6, MeOH). Spectroscopic properties identical with published data (Mori & Mori, 1987).

3.10. Methyl (2E,6E,10R)-10,11-dihydroxy-7,9,11-trimethyl-2,6-dodecadienoate (7)

Colorless oil. TLC: R_f 0.35; anisaldehyde: greenish yellow. $[\alpha]_D$ +8° (*c* 1.3); (Mori & Mori, 1987): $[\alpha]_D$ +18.9° (*c* 0.1, MeOH). Spectroscopic properties identical with published data (Mori & Mori, 1987; Waterman & Muhammad, 1985; Tane et al., 1988).

3.11. (S)- and (R)-MTPA-esters of 7

The esters were prepared according to reported procedures (Dale & Mosher, 1973). (*S*)-MTPA-7: ^{1}H-NMR: δ 1.13 (3H, *s*, Me-12), 1.17 (3H, *s*, C-11-Me), 1.56 (3H, *br s*, C-9-Me), 1.66 (1H, *m*, H-9a), 1.77 (1H, *m*, H-9b), 1.97 (2H, *m*, 2 × H-8), 2.16 (3H, *d*, J = 1.5 Hz, C-7-Me), 2.17 (4H, *m*, 2 × H-4, 2 × H-5), 3.57 (3H, *q*, J = 1 Hz, OMe), 3.68 (3H, *s*, COOMe), 4.98 (1H, *dd*, $J_1 = 10$, $J_2 = 2$ Hz, H-10), 5.05 (1H, *m*, H-6), 5.68 (1H, *br s*, H-2), 7.41 (3H, *m*, ar-H), 7.61 (2H, *m*, ar-H). (*R*)-MTPA-7: ^{1}H-NMR: δ 1.15 (3H, *s*, Me-12), 1.21 (3H, *s*, C-11-Me), 1.55 (3H, *br s*, C-9-Me), 1.60 (1H, *m*, H-9a), 1.68 (1H, *m*, H-9b), 1.86 (2H, m, 2 × H-8), 2.16 (3H, *d*, J = 1.5 Hz, C-7-Me), 2.17 (4H, *m*, 2 × H-4, 2 × H-5), 3.58 (3H, *q*, J = 1 Hz, OMe), 3.68 (3H, *s*, COOMe), 4.97 (1H, *dd*, $J_1 = 10$, $J_2 = 2$ Hz, H-10), 5.01 (1H, *m*, H-6), 5.69 (1H, *br s*, H-2), 7.41 (3H, *m*, ar-H), 7.64 (2H, *m*, ar-H).

3.12. 3,4,5-Trimethoxyphenol

Yellowish solid. TLC: R_f 0.41; anisaldehyde: orange. Identical with a purchased sample (Lancaster).

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