Naturally Occurring 5-Lipoxygenase Inhibitors. VI.¹⁾ Structures of Ardisiaquinones D, E, and F from *Ardisia sieboldii*

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New 1,4-benzoquinone derivatives, ardisiaquinones D (2), E (4), and F (5) along with the known ardisiaquinones A (1) and B (3) have been isolated from the leaves of *Ardisia sieboldii* (Myrsinaceae) and shown to be 5-lipoxygenase inhibitors. Their structures have been elucidated by spectroscopic analysis and chemical degradation. The degree of inhibition of 5-lipoxygenase activity by the ardisiaquinones and some derivatives of ardisiaquinone A is reported.

Key words *Ardisia sieboldii*; 1,4-benzoquinone; 5-lipoxygenase inhibitor; ardisiaquinone D; ardisiaquinone E; ardisiaquinone F

In the arachidonic acid cascade of prostaglandin biosynthesis, 5-lipoxygenase is an important enzyme catalyzing the oxygenation of arachidonic acid specifically at C-5, the initial step in the biosynthesis of the slow-reacting substances of anaphylaxis which are now known to be leukotrienes C₄, D₄, and E₄. A group of leukotrienes is regarded as one of the chemical mediators of bronchial asthma.²⁾ Hence, from a medicinal point of view it is important to search for a specific inhibitor of 5-lipoxygenase in natural products. We have already reported that some alkenyl-1,4-benzoquinones, ardisianones A and B,³⁾ and alkenylphenol, belamcandol A,⁴⁾ isolated from *Ardisia japonica* and *Belamcanda chinensis*, respectively, exhibit 5-lipoxygenase inhibitory activity. Previous results suggest that naturally occurring 1,4-benzoquinones could be candidates for evaluation of their 5-lipoxygenase inhibitory activity. Extensive study of the distribution of benzoquinone derivatives among Myrsinaceae plants by Natori *et al.*,⁵⁾ indicated the *Ardisia* species to be a rich source of benzoquinone derivatives. In fact, we have already reported that ardisiaquinone A (1), the main component of *Ardisia sieboldii*, is a potent 5-lipoxygenase inhibitor.¹⁾ These results encouraged us to reinvestigate the chemical constituents of *Ardisia sieboldii* collected on the island of Ishigaki during our search for analogs of ardisiaquinone A for structure function studies. Repeated chromatography of the methanol extract of its leaves resulted in the isolation of new 1,4-benzoquinones, 2, 4, and 5, designated as ardisiaquinones D, E, and F along with the known ardisiaquinones A (1) and B (3).^{6,7)} As expected, these benzoquinones strongly inhibited 5-lipoxygenase activity in the cytosol of guinea pig polymorphonuclear leukocytes. In this paper, we report the structures of these three new benzoquinones 2, 4, and 5, and their 5-lipoxygenase inhibitory activity.

Ardisiaquinone D (2), mp 88–90 °C, has the molecular formula C₃₁H₄₂O₈ [*m/z* 542.2878 (M⁺); Calcd 542.2879] suggesting the addition of an extra methyl group to ardisiaquinone A (1). The ultraviolet (UV) spectrum showed a dioxygenated benzoquinone chromophore at 284 and 420 nm.⁸⁾ The infrared (IR) spectrum revealed absorptions at 3370, 1660, and 1630 cm⁻¹ attributable to

hydroxy groups and the benzoquinone moiety, respectively, and the presence of the two hydroxy groups was also supported by the detection of temperature-variable proton signals, observed at δ_H 7.14 and 7.24 at 27 °C, in the ¹H-NMR spectrum. The ¹H-NMR spectrum of 2 contained singlet methyl and methoxy signals at δ_H 1.93 and 4.09, in addition to a series of signals, being made up of a methoxy at δ_H 3.86 (3H, s), olefinic protons at δ_H 5.33 (2H, t, *J* = 4.8 Hz) and 5.84 (1H, s), and methylenes integrated with 28H (δ_H 1.30–1.44 and 2.00–2.43), which were very similar to those of 1.¹⁾ Additionally, the ¹³C-nuclear magnetic resonance (¹³C-NMR) data (Table 1) of 2 in combination with the distortionless enhancement by polarization transfer

4 R = H

5 R = Me

Fig. 1

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(DEPT) indicated the presence of fourteen sp^2 carbon signals assignable to one disubstituted double-bond (δ_C 129.9) and two kinds of 1,4-benzoquinone units, half the signals of which were identical with those of the 1,4-benzoquinone ring in **1**, whereas the remaining six quaternary signals at δ_C 118.7, 122.7, 150.8, 157.2, 183.7, and 184.2 could be allocated to the carbons of a fully substituted 1,4-benzoquinone by the ^1H -detected multiple-bond heteronuclear multiple quantum coherence (HMBC) spectrum as shown in Fig. 2. Thus, the olefinic methyl proton signal at δ_H 1.93 correlated with C-1', C-6', and C-5', whereas the hydroxy proton signal at δ_H 7.14 showed clear cross peaks with C-1', C-2', and C-3', the latter two carbons in turn showed correlations with the methylene signals observed at δ_H 2.39. Additionally, it

Table 1. ^{13}C -NMR Data (100 MHz, CDCl_3) for Compounds **1**–**5**

Carbon	1	2	3	4	5
1	182.8	182.8	182.9	182.9	182.8
2	151.5	151.5	151.6	151.7	151.6
3	119.2	119.2	119.3	119.3	119.2
4	181.7	181.7	181.7	182.0	181.7
5	161.1	161.1	161.2	161.1	161.1
6	102.2	102.2	102.2	102.2	102.2
7	29.7	29.6	29.5	31.0	31.2
13	27.1	27.2	27.2	27.1	27.2
14	130.0	129.9	129.9	130.0	130.0
1'	182.8	184.2	181.7	156.7	154.6
2'	151.5	150.8	151.6	107.9	107.7
3'	119.2	118.7	116.1	146.0	142.0
4'	181.7	183.7	182.9	107.9	107.7
5'	161.1	157.2	161.1	156.7	154.6
6'	102.2	122.7	111.6	100.2	107.7
7'	29.7	29.7	29.7	35.8	35.5
13'	27.1	27.2	27.2	27.1	27.2
14'	130.0	129.9	129.9	130.0	130.0
C ₅ -OMe	56.8	56.7	56.8	56.8	56.8
C ₅ '-OMe	56.8	61.5	—	—	—
C ₆ '-Me	—	8.0	8.5	—	7.6

The carbon signals assignable for C-8—C-12 and C-8'—C-12': **1**: δ 22.6, 28.0, 29.2, 29.3, 29.5; **2**: δ 22.6, 28.0, 28.3, 29.2, 29.3, 29.4, 29.5; **3**: δ 22.4, 22.6, 28.0, 29.3, 29.4; **4**: δ 22.6, 28.0, 29.0, 29.1, 29.3, 29.4, 29.5, 29.6, 29.7; **5**: δ 22.6, 28.2, 28.3, 29.2, 29.3, 29.4, 29.5.

Fig. 2. Long Range C-H Correlations for the Left and Right 1,4-Benzoquinone Rings of **2** Based on HMBC ($J_{\text{C-H}} = 8.1 \text{ Hz}$)

Fig. 3

was evident that the two methoxy groups, which resonated at δ_H 3.86 and 4.09, were attached to C-5 and C-5', not only by HMBC (Fig. 2) but also by observation of the nuclear Overhauser effect (NOE) between the high-field methoxy signal and the singlet olefinic proton signal at δ_H 5.84. Furthermore, additional evidence supporting the presence of two types of *p*-benzoquinones was obtained from the prominent fragment ion peaks at m/z 168, 169, and 183 in the electron impact-mass spectrometry (EI-MS)⁷⁾ as shown in Fig. 3. The above spectral data showed that the two 1,4-benzoquinone rings present in **2** were the same as **1** and 3-alkenyl-2-hydroxy-5-methoxy-6-methyl-1,4-benzoquinone. Thus, taking the molecular formula into consideration, the two *p*-benzoquinone units were linked to the terminal positions of the C₁₆ long chain having one double-bond like ardisiaquinone A (**1**). Compound **2** was converted to the methoxy derivative **2a** by diazomethane. The sole double-bond on the C₁₆ linker in **2a** was oxidized with *m*-chloroperbenzoic acid followed by HIO₄ to give the two degraded products **2c** and **2d**, the spectral data of which showed equivalent structures and, thereby, the location of the double-bond must be at C-14 and 14'. The stereochemistry of the double-bond was assigned to *Z* from the diagnostic chemical shift of the allylic methylene carbon at δ 27.2.⁹⁾ Thus, these data corroborated that the structure of ardisiaquinone D (**2**) was (*Z*)-1-(3',6'-dioxo-2'-hydroxyl-5'-methoxycyclohexa-1',4'-dienyl)-16-(3',6'-dioxo-2'-hydroxyl-5'-methoxyl-4'-methylcyclohexa-1',4'-dienyl)-8-hexadecene.

Ardisiaquinone E (**4**), isolated as a viscous yellow oil, has the molecular formula C₂₉H₄₀O₆ determined by high resolution (HR) EI-MS. The UV and IR spectra of **4** showed the presence of hydroxy groups and a *p*-benzoquinone at 280 nm, and 3390, 1642 and 1610 cm⁻¹. The ^1H - and ^{13}C -NMR spectra of **4** revealed signals [δ_H 3.84 (3H, s, OCH₃), 5.83 (1H, s); δ_C : see Table 1] typical of a 3-alkenyl-2-hydroxy-5-methoxy-1,4-benzoquinone which is the common structural unit in **1** and **2**, and signals assignable to a symmetrical resorcinol-type benzene ring at δ_H 6.20 (1H, t, $J = 2.2 \text{ Hz}$) and 6.25 (2H, d, $J = 2.2 \text{ Hz}$), and δ_C 100.2 (C-6'), 107.9 (C-2', 4'), 146.0 (C-3'), and 156.7 (C-1', 5'), as well as signals due to the C₁₆ alkenyl linker at δ_H 1.29–1.55 (20H, m), 2.19 (4H, m), 2.44 (2H, t, $J = 7.7 \text{ Hz}$), and 2.47 (2H, t, $J = 7.7 \text{ Hz}$). These spectral data imply that ardisiaquinone E consists of a *p*-benzoquinone unit identical with that in **1** and the resorcinol part, both of which are presumably linked *via* the C₁₆ alkenyl chain containing one double-bond. This was supported by the detection of characteristic fragment ion peaks at m/z 168, 169, and m/z 123 and 124 in the EI-MS⁴⁾ as shown in Fig. 3, accounting for the rupture of the benzylic bonds of the alkenyl group, and by ob-

Chart 1. Degradation Products Obtained from **2a**, **4**, and **5** by Oxidative Cleavage of the Internal Olefin

servation of NOEs for the H-6 at δ_H 5.83, and the H-2' and 4' at δ_H 6.25 upon irradiation of the methoxy signal at δ_H 3.84 and the benzylic proton signal at δ_H 2.44, respectively. The location of the double-bond in the C₁₆ linker was found to be at C-14 and 14' by identification of the aldehyde **4a** [m/z 280 (M^+); δ_H 9.76 (1H, t, J = 2.2 Hz)], obtained from oxidative degradation of **4** by the same procedure as for **2**; its stereochemistry was also assigned as *Z* on the basis of the chemical shifts (δ_C 27.1) for the allylic methylene carbon. Accordingly, the structure of ardisiaquinone E (**4**) was assigned as (*Z*)-1-(3',6'-dioxo-2'-hydroxyl-5'-methoxycyclohexa-1',4'-dienyl)-16-(3',5'-dihydroxyphenyl)-8-hexadecene.

Ardisiaquinone F (**5**), mp 85–87 °C, has the molecular formula C₃₀H₄₂O₆ (m/z 498.2972, Calcd 498.2981), and its UV and IR spectra indicated the presence of hydroxy groups and a 1,4-benzoquinone moiety. The ¹H-NMR spectrum of **5** was closely related to that of ardisiaquinone E (**4**) except for an olefinic methyl at δ_H 2.10 (3H, s) and a 2H singlet aromatic proton signal at δ_H 6.25, indicating that there was one methyl group at δ_C 7.6 (q) at the C-6' position on the resorcinol ring in **4**. This gross structure was consistent with the other spectral data as follows; ¹³C-NMR (Table 1), EI-MS [m/z 168, 169, 137, 138 (base)], and NOE [δ_H 5.83/3.85 (OCH₃), δ_H 6.25/2.44 (benzylic H)]. The stereochemistry and position of the internal double-bond in the C₁₆ alkenyl chain linking both rings was determined as *Z* (δ_C 27.2 for C-13 and 13') and located at C-14 and 14' by identification of **4a** degraded from **5** according to the same oxidative procedure as for **4** (Chart 1). Thus, the structure of ardisiaquinone F (**5**) was represented as (*Z*)-1-(3',6'-dioxo-2'-hydroxyl-5'-methoxycyclohexa-1',4'-dienyl)-16-(3',5'-dihydroxyl-4'-methylphenyl)-8-hexadecene.

The 5-lipoxygenase inhibitory activity of the new compounds isolated during the present study and the previously known 1,4-benzoquinone derivatives was evaluated using enzyme from guinea pig peritoneal polymorphonuclear leukocytes according to the method of Yamamoto *et al.*¹⁰ The degree of inhibition (%) of 5-lipoxygenase by ardisiaquinone A (**1**) and its derivatives **1a**–**c**, and ardisiaquinones D (**2**), B (**3**), E (**4**), F (**5**), and some alkenyl 1,4-benzoquinones **6**–**8**^{3,11} is listed in Table 2. Ardisiaquinone A (**1**), which exhibited 43% inhibition of 5-lipoxygenase activity at 0.1 μ M was the

Table 2. Inhibition (%) of 5-Lipoxygenase in the Cytosol of Guinea Pig Polymorphonuclear Leukocytes by Ardisiaquinones and Their Derivatives

Compound	Inhibition (%)			
	Concentration (μ M)			
	0.1	0.3	1.0	3.0
1	43	63	94	96
1a	7	54	88	91
1b	17	41	88	97
1c	66	92	96	96
2	4	44	86	—
3	21	—	89	89
4	24	28	70	80
5	7	29	58	—
6	0	0	16	—
7	10	22	67	—
8	0	0	10	13
NDGA ^{a)}	0	24	—	—

a) Nor-dihydroguaiaretic acid.

most potent inhibitor of all the dimeric ardisiaquinones. The derivative **1c** containing an epoxide ring exhibited the strongest inhibitory activity of all the analogs of **1**. The methylated and dihydrogenated derivatives, **1a** and **1b**, however, exhibited decreased inhibitory activity, presumably due to a slight loss of hydrophilicity and free movement of both *p*-benzoquinone units spatially oriented in the same direction by the internal *Z* olefin. On the other hand, in comparison with the simple alkenyl 1,4-benzoquinones **6**–**8**, they were much less potent inhibitors than the dimeric 1,4-benzoquinones **1**–**5** except for maesanin (**7**).¹¹ The structural variation among these eight natural products and the three analogs of **1** allowed us to propose preliminary structure–activity relationships. It appears that one of the two dioxygenated 1,4-benzoquinone rings in ardisiaquinone A is essential, the hydroxy group at C-2 is somewhat less critical, and the nature of the other ring at the terminal position and the length of the linker are open to considerable variation.

Ardisiaquinone A¹⁾ is a potent inhibitor of 5-lipoxygenase and exhibit almost identical activity to that of the clinically useful AAA-861.¹²⁾ Hence, synthesis of derivatives of ardisiaquinones may lead to compounds with increased potency.¹³⁾

Experimental

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. UV spectra were recorded on a Hitachi 340 spectrophotometer. IR spectra were measured on a Jasco A-2-2 spectrophotometer. ^1H - and ^{13}C -NMR spectra were obtained at 400 or 200 MHz (^1H -NMR) and 100.16 MHz (^{13}C -NMR) using JEOL GX-400 and Varian Unity 200 instruments. Chemical shift values were expressed in ppm downfield from tetramethylsilane as an internal standard. The MS were recorded on a JEOL AX-500 instrument. Silica-gel (Wako, C-300) was used for column chromatography. Silica-gel F₂₅₄ (Merck) was used for analytical (0.25 mm) and preparative (0.5 mm) thin-layer chromatographies, and spots were visualized under UV (254 nm) light and by spraying with 40% $\text{CeSO}_4\text{-H}_2\text{SO}_4$ followed by heating.

Extraction and Purification Dried and powdered leaves (1.23 kg) of *Ardisia sieboldii* collected on Ishigaki island were immersed three times in methanol at room temperature for 3 d. Combined extracts were evaporated *in vacuo* to give a gummy extract (138 g), which was partitioned between *n*-hexane and water-methanol (4:1). The resultant water-methanol phase was extracted three times with benzene. The benzene soluble portion (37.8 g) was chromatographed over silica-gel eluting with benzene-EtOAc (8:1) and benzene-EtOAc (4:1). The fraction eluted with benzene-EtOAc (8:1) was rechromatographed on silica-gel with CHCl_3 to give ardisiaquinone D (2) (172 mg) as crystals. The precipitate which was formed from the fraction eluted with benzene-EtOAc (4:1) was recrystallized from $\text{C}_2\text{H}_5\text{OH}$ -benzene to give ardisiaquinone A (1) (2.5 g) and the filtrate was chromatographed on silica-gel using a stepwise gradient [CHCl_3 , $\text{CHCl}_3\text{-CH}_3\text{OH}$ (50:1), and $\text{CHCl}_3\text{-CH}_3\text{OH}$ (10:1)] to give ardisiaquinone B (3) (148 mg), ardisiaquinone E (4) (140 mg), and ardisiaquinone F (5) (135 mg).

Ardisiaquinone D (2) Yellow-orange powder (from benzene-*n*-hexane), mp 88–90 °C. EI-MS m/z (rel. int.): 542 (M^+ , 78), 514 (23), 360 (14), 183 (100), 169 (95), 168 (96). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm: 284 (ϵ 34900), 420 (ϵ 800). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3370 (OH), 1660, 1630. ^1H -NMR (400 MHz, CDCl_3) δ : 1.30 (16H, m), 1.44 (4H, m), 1.93 (3H, s, $\text{C}_6\text{-Me}$), 2.01 (4H, m, H-13, 13'), 2.39 (2H, t, $J=7.8$ Hz, H-7'), 2.43 (2H, t, $J=7.7$ Hz, H-7), 3.86 (3H, s, $\text{C}_5\text{-OMe}$), 4.09 (3H, s, $\text{C}_5\text{-OMe}$), 5.33 (2H, t, $J=4.8$ Hz, H-14, 14'), 5.84 (1H, s, H-6), 7.14 (1H, s, $\text{C}_2\text{-OH}$), 7.24 (1H, s, $\text{C}_2\text{-OH}$). ^{13}C -NMR: see Table 1. HR EI-MS m/z : 542.2878 (M^+), Calcd 542.2879 for $\text{C}_{31}\text{H}_{42}\text{O}_8$.

Oxidative Cleavage of the Double Bond in 2 Ardisiaquinone (2) (9 mg) was methylated with diazomethane to give the methylated derivative **2a** (9.2 mg), which was dissolved in CH_2Cl_2 (3 ml). To this solution was added *m*-chloroperoxybenzoic acid (4 mg) and then the reaction mixture was left standing at room temperature for 4 h. Ether was added to the reaction mixture and then the organic layer was washed with sat. NaHCO_3 sol. and sat. NaCl sol. After being dried over MgSO_4 , the organic layer was evaporated *in vacuo* to give a residue, which was purified by prep. TLC (CHCl_3) giving rise to an epoxide **2b** (3.3 mg). To a solution of this epoxide in THF-water (2 ml, 1:1) was added HIO_4 (2.5 mg) and the reaction mixture was stirred at 45 °C for 2 h. Ether was added and the organic layer was washed with sat. NaHCO_3 sol. and sat. NaCl sol. After drying over MgSO_4 , the organic layer was evaporated *in vacuo* to leave a residue, which was purified by prep. TLC (CHCl_3) to yield the aldehydes **2c** (0.5 mg) and **2d** (0.6 mg). **2c**: EI-MS m/z : 294, 279, 167, 153. ^1H -NMR (200 MHz, CDCl_3) δ : 1.25–1.55 (m), 2.41 (2H, m), 3.85 (3H, s), 4.05 (3H, s), 9.75 (1H, t, $J=2.2$ Hz). **2d**: EI-MS m/z : 308, 293, 280, 197, 181, 167, 153. ^1H -NMR (200 MHz, CDCl_3) δ : 1.20–1.55 (m), 1.98 (3H, s), 2.44 (2H, m), 4.04 (3H, s), 4.08 (3H, s), 9.76 (1H, t, $J=1.8$ Hz).

Ardisiaquinone E (4) Yellow colored oil. EI-MS m/z (rel. int.): 484 (M^+ , 100), 169 (28), 168 (38), 124 (39), 123 (28). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm: 280 (ϵ 35800). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3390 (OH), 1642, 1610. ^1H -NMR (400 MHz, CDCl_3) δ : 1.29 (16H, m), 1.45 (2H, m), 1.55 (2H, m), 2.19 (4H, m, H-13, 13'), 2.44 (2H, t, $J=7.7$ Hz, H-7'), 2.47 (2H, t, $J=7.7$ Hz, H-7), 3.84 (3H, s, $\text{C}_5\text{-OMe}$), 5.34 (2H, t, $J=4.6$ Hz, H-14, 14'), 5.83 (1H, s, H-6), 6.20 (1H, t, $J=2.2$ Hz, H-6'), 6.25 (2H, d, $J=2.2$ Hz, H-2', 4'). ^{13}C -NMR: see Table 1. HR EI-MS m/z : 484.2821 (M^+), Calcd 484.2825 for $\text{C}_{29}\text{H}_{40}\text{O}_6$.

Oxidative Cleavage of the Double Bond in 4 The double-bond of **4** (7 mg) was cleaved by the same procedure as for **2**, affording the aldehyde **4a** (1.7 mg) as an oil. EI-MS m/z : 280 (M^+). ^1H -NMR (200 MHz, CDCl_3) δ : 2.43 (2H, t, $J=7.0$ Hz), 3.85 (3H, s), 5.83 (1H, s), 9.76 (1H, t, $J=2.2$ Hz).

Ardisiaquinone F (5) Orange powder (from benzene-EtOAc), mp 85–87 °C. EI-MS m/z (rel. int.): 498 (M^+ , 70), 169 (50), 168 (78), 138 (100), 137 (97). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm: 283 (ϵ 48900). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3375 (OH), 1642, 1618. ^1H -NMR (400 MHz, CDCl_3) δ : 1.29 (16H, m), 1.60 (2H, m), 1.90 (2H, m), 2.00 (4H, m, H-13, 13'), 2.10 (3H, s, $\text{C}_6\text{-Me}$), 2.44 (2H, t, $J=7.8$ Hz, H-7'), 2.47 (2H, t, $J=7.7$ Hz, H-7), 3.85 (3H, s, $\text{C}_5\text{-OMe}$), 4.98 (2H, br s, OH), 5.33 (2H, t, $J=6.5$ Hz, H-14, 14'), 5.83 (1H, s, H-6), 6.25 (2H, s, H-2', 4'). ^{13}C -NMR: see Table 1. HR EI-MS m/z : 498.2972 (M^+), Calcd 498.2981 for $\text{C}_{30}\text{H}_{42}\text{O}_6$.

Oxidative Cleavage of the Double Bond in 5 The double-bond of **5** (5 mg) was cleaved by the same procedure as for **4**, affording the aldehyde **4a** (0.7 mg) as an oil.

Methylation of Ardisiaquinone A (1) To a solution of **1** (10 mg) in CH_3OH -ether (3 ml, 2:1) was added an excess ethereal solution of diazomethane at 0 °C. The mixture remained at room temperature overnight. Solvent was removed *in vacuo* to give an oil, which was purified using a short silica-gel column (CHCl_3) to afford **1a** (9.2 mg) as an oil. EI-MS m/z (rel. int.): 556 (M^+ , 100), 183 (41), 153 (31). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1657, 1599. ^1H -NMR (400 MHz, CDCl_3) δ : 1.30 (20H, m), 1.99 (4H, m), 2.43 (4H, t, $J=7.4$ Hz), 3.82 (6H, s), 4.05 (6H, s), 5.34 (2H, t, $J=4.6$ Hz), 5.73 (2H, s). HR EI-MS m/z : 556.3055 (M^+), Calcd 556.3036 for $\text{C}_{32}\text{H}_{44}\text{O}_8$.

Catalytic Hydrogenation of 1 A solution of **1** (5 mg) in $\text{C}_2\text{H}_5\text{OH}$ (1 ml) was hydrogenated over 10% Pd-C (1 mg) under hydrogen at normal pressure for 2 h. After filtering off the catalyst, the filtrate was evaporated to give **1b** (5.1 mg) as an oil. EI-MS m/z (rel. int.): 530 (M^+ , 86), 502 (100), 169 (38). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3341 (OH), 1635, 1599. ^1H -NMR (400 MHz, CDCl_3) δ : 1.31 (28H, m), 2.44 (4H, t, $J=7.1$ Hz), 3.86 (6H, s), 5.84 (2H, s). HR EI-MS m/z : 530.2864 (M^+), Calcd 530.2879 for $\text{C}_{30}\text{H}_{42}\text{O}_8$.

Epoxidation of 1 A mixture of **1** (20 mg), *m*-chloroperoxybenzoic acid (12 mg), and CH_2Cl_2 (3 ml) was left standing at room temperature for 2 h. Ether was added to the reaction mixture and then the organic layer was washed with sat. NaHCO_3 sol. and sat. NaCl sol. After drying over MgSO_4 , the organic layer was evaporated *in vacuo* to yield an epoxide **1c** (22 mg) as an oil. EI-MS m/z (rel. int.): 544 (M^+ , 27), 516 (26), 282 (35), 193 (26), 169 (100). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3331 (OH), 1645, 1608. ^1H -NMR (400 MHz, CDCl_3) δ : 1.48–2.14 (24H, m), 2.44 (4H, t, $J=4.6$ Hz), 2.91 (2H, m), 3.86 (6H, s), 5.84 (2H, s). HR EI-MS m/z : 544.2700 (M^+), Calcd 544.2673 for $\text{C}_{30}\text{H}_{40}\text{O}_9$.

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- Total syntheses of ardisiaquinones D (2), E (4), and F (5) have been already achieved by us. Their synthetic detail will be reported in due time.