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Isolation and Characterization of Cardiac Steroids from Seeds of *Elaeopendron glaucum* Pers. Structures of Elaeodendrosides A, D, E, H, I, J and Elaeodendrogenin[1)]

Kazutake Shimada,[a] Tomoko Kyuno,[a] Toshio Nambara,*,[a] and Itsuo Uchida[b,2)]

Pharmaceutical Institute, Tohoku University,[a] Aobayama, Sendai 980, Japan and Department of Chemistry, University of Virginia,[b] Charlottesville, Va. 22901, U.S.A.

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Six cardiac glycosides having a methylenedioxy group in the sugar moiety, elaeodendroside A, D, E, H, I and J, were isolated from seeds of *Elaeodendron glaucum* Pers. Their structures were elucidated on the basis of chemical correlation with elaeodendroside A, which was characterized by X-ray analysis. A new cradiac steroid named elaeodendrogenin was also isolated from the same plant materials and its structure was established by direct comparison with a synthetic sample obtained from digitoxigenin. The cardiac activities of these compounds were tested with Straub's preparation.

Keywords——*Elaeodendron glaucum*; Celastraceae; cardiac glycoside; elaeodendroside; doubly linked sugar; elaeodendrogenin; cardiac activity

In the course of a continuing search for tumor inhibitors and cardiac steroids from natural sources, we found that the 95% ethanol extract of seeds of *Elaeodendron glaucum* Pers. (Celastraceae) showed significant inhibitory activity *in vitro* against cells derived from human nasopharynx carcinoma (KB).[3)] Chloroform–water partition of the alcoholic extract followed by 90% methanol–hexane partition of the chloroform extract and column chromatography of the 90% methanol extract on silica gel gave several anti-KB active fractions. Each fraction was subjected to dry column chromatography or preparative thin-layer chromatography (TLC) on silica gel. Twenty kinds of anti-KB active compounds exhibiting positive Kedde reaction were isolated by this method.

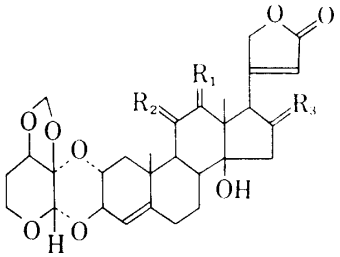
Elaeodendroside A (**1**), mp 299—300°C, was separated as colorless prisms. Elemental analysis and high resolution mass spectral data provided the molecular formula $C_{29}H_{36}O_{10}$. The complete structure was determined as **1** by direct single-crystal X-ray analysis.[4)]

Elaeodendroside J (**2**), mp 274—276°C (dec.), was separated as colorless prisms. When adsorbed on alumina or silica gel in methanol–acetone for a week,[5,6)] **1** underwent ketol rearrangement to yield **2**, which was identical with the above product. In the proton nuclear magnetic resonance (^{1}H-NMR) spectrum, **2** exhibited a singlet signal at 4.15 ppm,[7)] which lent support to the assigned structure.

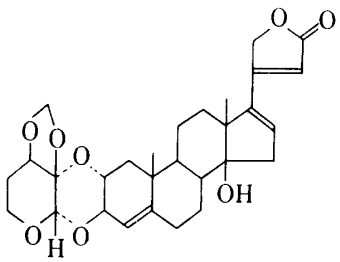
Elaeodendroside D (**3**), mp 275—285°C (dec.), was isolated as colorless prisms. Inspection of the high resolution mass and ^{1}H-NMR spectra permitted us to assign the structure **3** to elaeodendroside D. The structure was definitely established by direct comparison with a synthetic sample derived from **1**. Reduction of **1** with sodium borohydride gave two diols (**4**, **5**). Compound **4** proved to be identical with one of the products obtained from **2** by borohydride reduction. These results indicated that **4** and **5** possessed the 11α,12α- and 11α,-12β-diol structures, respectively. Compound **4** was transformed into the monomesylate (**6**) in the usual manner. Treatment of **6** with sodium iodide and zinc dust in diglyme[8)] provided the 12-ketone (**7**) as colorless prisms. In the ^{1}H-NMR spectrum, **7** exhibited the signals of 18- and 19-methyl groups at 1.08 and 1.22 ppm, indicating the presence of an oxo group at C-12 rather than at C-11. The 12-ketone was transformed into the *p*-tosylhydrazone which in turn was reduced with sodium borocyanohydride in dimethylformamide–sulfolane.[9)] The compound thus obtained proved to be identical with **3**.

Elaeodendroside E (**8**), mp 283—290°C (dec.), was separated as colorless prisms. The high resolution mass spectrum and elemental analysis data permitted us to assign the molecular formula $C_{31}H_{40}O_{10}$ to **8**. In the ^{1}H-NMR spectrum, **8** exhibited signals at 2.00, 2.60, 3.25 and 5.60 ppm. These data suggested the presence of an acetoxyl group at the 16β-position.[10] Hydrolysis of **8** with potassium bicarbonate in methanol under mild conditions afforded desacetylelaeodendroside E (**9**) as colorless prisms. Compound **9** was readily and quantitatively transformed into the cyclic phenylboronate, indicating the existence of a *cis*-glycol structure.[11] When adsorbed on alumina in benzene at 60°C for 5 h, **8** was converted into elaeodendroside H (**15**), mp 293—295°C (dec.). Partial hydrogenation of **15** over 5% palladium-on-charcoal provided 17α-elaeodendroside D together with a small amount of **3**. The major product was also obtained from **3** by the procedure described by Merkel *et al.*[12] On the basis of these results elaeodendroside E was unequivocally identified as 16β-acetoxyelaeodendroside D (**8**).

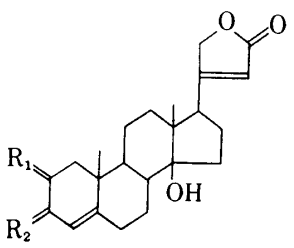
Compound **15** was also obtained from the natural source and its structure was confirmed by direct comparison with the Δ^{16} compound derived from **8**. Compound **8** underwent no alteration during the isolation procedure using silica gel as an adsorbent. Accordingly, the possibility that **15** might be an artifact formed from **8** was ruled out.



1: $R_1 = O$, $R_2 = \langle^{H}_{OH}$, $R_3 = H_2$
2: $R_1 = \langle^{H}_{OH}$, $R_2 = O$, $R_3 = H_2$
3: $R_1 = R_2 = R_3 = H_2$
4: $R_1 = R_2 = \langle^{H}_{OH}$, $R_3 = H_2$
5: $R_1 = \langle^{OH}_{H}$, $R_2 = \langle^{H}_{OH}$, $R_3 = H_2$
6: $R_1 = \langle^{H}_{OH}$, $R_2 = \langle^{H}_{OMs}$, $R_3 = H_2$
7: $R_2 = O$, $R_2 = R_3 = H_2$
8: $R_1 = R_2 = H_2$, $R_3 = \langle^{OAc}_{H}$
9: $R_1 = R_2 = H_2$, $R_3 = \langle^{OH}_{H}$
10: $R_1 = H_2$, $R_2 = \langle^{H}_{OH}$, $R_3 = H_2$
11: $R_1 = H_2$, $R_2 = O$, $R_3 = H_2$
12: $R_1 = \langle^{H}_{OAc}$, $R_2 = O$, $R_3 = H_2$
13: $R_1 = H_2$, $R_2 = \langle^{H}_{OAc}$, $R_3 = H_2$
14: $R_1 = R_2 = O$, $R_3 = H_2$



15



16: $R_1 = \langle^{H}_{OAc}$, $R_2 = \langle^{OH}_{H}$
17: $R_1 = \langle^{H}_{OAc}$, $R_2 = \langle^{OAc}_{H}$
18: $R_1 = \langle^{H}_{OAc}$, $R_2 = O$
19: $R_1 = H_2$, $R_2 = O$
20: $R_1 = \langle^{OAc}_{H}$, $R_2 = O$
21: $R_1 = \langle^{H}_{OH}$, $R_2 = \langle^{OH}_{H}$

Chart 1

Elaeodendroside I (**10**), mp 299—300°C (dec.), was separated as colorless leaflets. The high resolution mass spectrum and elemental analysis data provided the molecular formula $C_{29}H_{38}O_9$. Oxidation of **10** with pyridinium chlorochromate in dichloromethane gave the 11-ketone (**11**) as colorless prisms. The structural assignment was completely established by direct comparison with a synthetic sample obtained from **2**. Usual acetylation of **2** with acetic anhydride and pyridine afforded the 12-acetate (**12**). Elimination of the acetoxyl group by reduction with zinc dust in acetic acid[13] yielded the 11-ketone (**11**) which was identical with the compound derived from **10**. The configurational assignment of the 11α-hydroxyl group in **10** was supported by the chemical shifts of angular methyl groups in the ^{1}H-NMR spectrum[14] and the fact that **10** was easily converted into the acetate (**13**). Based upon these data, elaeodendroside I was unambiguously identified as **10**.

Elaeodendrogenin (**16**), mp 258—262°C, was isolated as colorless leaflets. Elemental analysis permitted us to assign the molecular formula $C_{25}H_{34}O_6$ to **16**. Usual acetylation with acetic anhydride and pyridine yielded the diacetate (**17**) as colorless leaflets. Nuclear Overhauser effect (NOE) (*ca.* 30%) observed between the 19-methyl group and 2-hydrogen, as well as the coupling constants ($J_{3,4}$=0 Hz, $J_{3,2}$=10 Hz), lent support to the assignment of the 2α,3β-glycol 2-monoacetate structure to **16**.[11] When treated with manganese dioxide, **16** was readily converted to the Δ^4-3-ketone (**18**). In addition, NOE (*ca.* 20%) was observed between the 19-methyl group and 2-hydrogen in **18**. The circular dichroism (CD) curve of **18** in methanol showed a negative Cotton effect with an extremum at 325 nm. These data strongly implied the presence of an acetoxyl group at the 2α-position.[15] The structure of **16** was definitely estabilished by direct comparison with a synthetic sample. Oxidation of anhydroperiplogenone (**19**)[16] with lead tetraacetate gave 2β-acetoxyanhydroperiplogenone (**20**), which in turn was epimerized by refluxing it with potassium acetate in acetic acid[17] and then reduced with sodium borohydride.[18] On the basis of these results, elaeodendrogenin was unequivocally identified as **16**.

The cardiac activities of the newly isolated steroids and their derivatives were tested with isolated frog heart (Straub's preparation).[19] The results obtained are listed in Table I. Elaeodendrosides A, D, E, and I showed almost identical activity, that is approximately one-third of that of digitoxigenin. The compounds (**14**, **4** and **5**) having the 11,12-diketone or 11,12-diol partial structure exhibited somewhat less activity. Elaeodendroside J was much less toxic than elaeodendroside A. These data suggested that the cardiac activities of these compounds were significantly influenced by the substituent in ring C.[20] Comparison of the

Table I. Biological Activities of Cardiac Steroids

Compound	Cardiac activity RP[a]	Cytotoxicity ED_{50} (μg/ml)
Digitoxigenin	1	
Elaeodendroside A (**1**)	0.3	0.13
D (**3**)	0.3	
E (**8**)	0.3	0.23
I (**10**)	0.3	0.029
Compound **7**	0.3	
11	0.3	
14	0.09—0.06	
4	0.09—0.06	
5	0.09—0.06	
9	0.09—0.06	
21	0.09—0.06	
Elaeodendroside J (**2**)	$<$ 0.01	0.49
H (**15**)	$\ll$ 0.01	

a) RP = relative potency. Digitoxigenin was taken as a standard (1.0). RP is shown on molar basis.

cardiac activities of elaeodendroside E, the desacetyl derivative (**9**) and elaeodendroside H was indicative of the significance of the C-16 substituent. Desacetylelaeodendrogenin (**21**) exhibited much less activity than digitoxigenin. These data implied that the 2α,3β-dihydroxy-4-ene structure may significantly depress the cardiac activity.[20]

Further structural elucidation studies on other cardiac steroids are being conducted in these laboratories and the details will be reported elsewhere in the near future.

Experimental

All melting points were taken on a micro hot-stage apparatus and are uncorrected. Optical rotations and CD spectra were measured with a JASCO DIP-4 automatic polarimeter and a JASCO J-400X optical rotation spectrometer, respectively. Low and high resolution mass spectra were run on Hitachi M-52 and JEOL JMS-01SG-2 spectrometers, respectively. High resolution mass spectral measurements using chemical ionization (CI) with methane were carried out with a AEI Model MS-902 spectrometer. ^{1}H-NMR spectra were recorded on a JEOL PS-100 spectrometer at 100 MHz using tetramethylsilane as an internal standard. Abbreviations used: s=singlet, d=doublet, t=triplet, q=quartet, and m=multiplet. For preparative thin-layer chromatography (TLC), silica gel HF_{254} (E. Merck AG, Darmstadt) and for column chromatography silica gel (70—230 mesh) (E. Merck AG) were used. Aluminum oxide 90 (E. Merck AG) was used as a catalyst for ketol rearrangement and elimination reactions.

Extraction of Steroidal Components——Seeds (5 kg) of *Elaeodendron glaucum* Pers. collected in India in March, 1975, were extracted with EtOH in a Soxhlet extractor. The ethanolic layer was concentrated *in vacuo*, and the residue was partitioned in a $CHCl_3$–H_2O system. The organic layer was concentrated *in vacuo*, and the residue was again partitioned in a 90% MeOH–hexane system. The methanolic layer was concentrated *in vacuo*, and the residue (90 g) was chromatographed repeatedly on silica gel using AcOEt–benzene, MeOH–ether, or MeOH–$CHCl_3$ as eluents. Purification of the eluate by preparative TLC using benzene–AcOEt, $CHCl_3$–acetone, benzene–ether, or $CHCl_3$–MeOH gave the following cardiac steroids.[21]

Elaeodendroside A (**1**) (300 mg). mp 299—300°C, colorless prisms (from MeOH–acetone), $[\alpha]_D^{24}$ +96.0° (c=0.18, $CHCl_3$). *Anal.* Calcd for $C_{29}H_{36}O_{10}$: C, 63.96; H, 6.66. Found: C, 63.94; H, 6.68. High resolution MS (CI) m/z: Found: 545.2371. Calcd for $C_{29}H_{37}O_{10}$ $(M+H)^+$=545.2386. ^{1}H-NMR ($CDCl_3$) δ: 1.15 (3H, s, 18-CH_3), 1.43 (3H, s, 19-CH_3), 2.50 (1H, dd, J=14, 3.2 Hz, 1β-H), 3.60—4.30 (5H, m, 2β-H, 3′α-H, 5′-CH_2, 17α-H), 4.38 (1H, br d, J=8 Hz, 3α-H), 4.45 (1H, d, J=12 Hz, 11β-H), 4.67 (1H, s, 1′β-H), 4.90 (2H, m, 21-CH_2), 5.16 (2H, ABq, -OCH_2O-),[22] 5.30 (1H, br s, 4-H), 6.10 (1H, br s, 22-H).

Elaeodendroside J (**2**) (22 mg). mp 274—276°C (dec.), colorless prisms (from ether), $[\alpha]_D^{19}$ +10.0° (c=0.05, $CHCl_3$). *Anal.* Calcd for $C_{29}H_{36}O_{10}$: C, 63.96; H, 6.66. Found: C, 63.94; H, 6.49. High resolution MS (CI) m/z: Found: 545.2371. Calcd for $C_{29}H_{37}O_{10}$ $(M+H)^+$=545.2386. ^{1}H-NMR ($CDCl_3/D_2O$) δ: 1.15 (3H, s, 18- or 19-CH_3), 1.19 (3H, s, 18- or 19-CH_3), 3.60—4.10 (5-H, m, 2β-H, 3′α-H, 5′-CH_2, 17α-H), 4.15 (1H, s, 12β-H), 4.45 (1H, d, J=8 Hz, 3α-H), 4.65 (1H, s, 1′β-H), 5.15 (4H,m, -OCH_2O-, 21-CH_2), 5.30 (1H, br s, 4-H), 5.85 (1H, br s, 22-H).

Elaeodendroside D (**3**) (10 mg). mp 275—285°C (dec.), colorless prisms (from CH_2Cl_2–ether), $[\alpha]_D^{10}$ +30.0° (c=0.10, $CHCl_3$). *Anal.* Calcd for $C_{29}H_{38}O_8$: C, 67.68; H, 7.44. Found: C, 67.75; H, 7.54. High resolution MS m/z: Found: 514.2608. Calcd for $C_{29}H_{38}O_8$ $(M)^+$=514.2565. ^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, s, 18-CH_3), 1.15 (3H, s, 19-CH_3), 2.75 (1H, br d, J=8 Hz, 17α-H), 3.50—4.20 (4H, m, 3′α-H, 5′-CH_2, 2β-H), 4.40 (1H, d, J=9 Hz, 3α-H), 4.66 (1H, s, 1′β-H), 4.88 (2H, m, 21-CH_2), 5.16 (2H, ABq, -OCH_2O-), 5.20 (1H, s, 4-H), 5.86 (1H, br s, 22-H).

Elaeodendroside E (**8**) (70 mg). mp 283—290°C (dec.), colorless prisms (from CH_2Cl_2–MeOH), $[\alpha]_D^{21}$ +7.9° (c=0.14, $CHCl_3$). *Anal.* Calcd for $C_{31}H_{40}O_{10}$: C, 65.02; H, 7.04. Found: C, 64.64; H, 7.00. High resolution MS (CI) m/z: Found: 573.2700. Calcd for $C_{31}H_{41}O_{10}$ $(M+H)^+$=573.2699. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (3H, s, 18-CH_3), 1.15 (3H, s, 19-CH_3), 2.00 (3H, s, $OCOCH_3$), 2.60 (1H, dd, J=17, 10 Hz, 15α-H), 3.25 (1H, d, J=10 Hz, 17α-H), 3.60—4.20 (4H, m, 3′α-H, 5′-CH_2, 2β-H), 4.45 (1H, d, J=8 Hz, 3α-H), 4.70 (1H, s, 1′β-H), 4.95 (2H, m, 21-CH_2), 5.22 (2H, ABq, -OCH_2O-), 5.25 (1H, s, 4-H), 5.60 (1H, dt, J=10, 2 Hz, 16α-H), 6.03 (1H, br s, 22-H).

Elaeodendroside H (**15**) (30 mg). mp 293—295°C (dec.), color ess prisms (from ether). $[\alpha]_D^{15.5}$ +166.7° (c=0.12, $CHCl_3$). UV λ_{max}^{MeOH} 270 nm. *Anal.* Calcd for $C_{29}H_{36}O_8$: C, 67.95; H, 7.08. Found: C, 67.90; H, 7.18. ^{1}H-NMR ($CDCl_3$) δ: 1.17 (3H, s, 19-CH_3), 1.31 (3H, s, 18-CH_3), 3.50—4.20 (4H, m, 3′α-H, 5′-CH_2, 2β-H), 4.39 (1H, d, J=8 Hz, 3α-H), 4.66 (1H, s, 1′β-H), 4.95 (2H, br s, 21-CH_2), 5.16 (2H, ABq, -OCH_2O-), 5.20 (1H, br s, 4-H), 5.94 (1H, br s, 22-H), 6.07 (1H, br s, 16-H).

Elaeodendroside I (**10**) (50 mg). mp 299—300°C (dec.), colorless leaflets (from acetone-ether), $[\alpha]_D^{21}$ +44.3° (c=0.14, $CHCl_3$). *Anal.* Calcd for $C_{29}H_{38}O_9 \cdot 1/2H_2O$: C, 64.55; H, 7.29. Found: C, 64.42; H, 7.10. High resolution MS (CI) m/z: Found: 531.2585. Calcd for $C_{29}H_{39}O_9$ $(M+H)^+$=531.2594. ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, s, 18-CH_3), 1.32 (3H, s, 19-CH_3), 2.50 (1H, dd, J=3.2, 14 Hz, 1β-H), 2.90 (1H, br d, J=10 Hz, 17α-H), 3.50—4.20 (5H, m, 3′α-H, 5′-CH_2, 2β-H, 11β-H), 4.50 (1H, d, J=10 Hz, 3α-H), 4.75 (1H, s, 1′β-H), 4.95 (2H, m, 21-CH_2), 5.25 (2H, ABq, -OCH_2O-), 5.35 (1H, br s, 4-H), 5.95 (1H, br s, 22-H).

Elaeodendrogenin (**16**) (30 mg). mp 258—262°C, colorless leaflets (from acetone–ether), $[\alpha]_D^{20}$ −21.1° (c=0.10, $CHCl_3$). *Anal.* Calcd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.36; H, 8.18. High resolution MS *m/z*: Found: 370.2115. Calcd for $C_{23}H_{30}O_4$ (M–AcOH)$^+$=370.2143. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, s, 18-CH_3), 1.15 (3H, s, 19-CH_3), 2.11 (3H, s, $OCOCH_3$), 2.76 (1H, m, 17α-H), 4.20 (1H, d, J=10 Hz, 3α-H), 4.80 (1H, m, 2β-H), 4.85 and 5.00 (each 1H, each dd, J=15, 2 Hz, 21-CH_2), 5.22 (1H, br s, 4-H), 5.88 (1H, br s, 22-H).

Preparation of Elaeodendrogenin Acetate (**17**)——Compound **16** (5 mg) was dissolved in Ac_2O–pyridine (1: 1) (2 ml) and the solution was allowed to stand at room temperature for 12 h. The reaction mixture was treated in the usual manner. Recrystallization of the crude product from ether gave **17** (3 mg) as colorless leaflets. mp 225—230°C, $[\alpha]_D^{20}$ −45.5° (c=0.06, $CHCl_3$). *Anal.* Calcd for $C_{27}H_{36}O_7$: C, 68.62; H, 7.68. Found: C, 68.58; H, 7.92. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, s, 18-CH_3), 1.18 (3H, s, 19-CH_3), 2.03 (3H, s, $OCOCH_3$), 2.06 (3H, s, $OCOCH_3$), 2.75 (1H, m, 17α-H), 4.85 and 5.00 (each 1H, each dd, J=15, 2 Hz, 21-CH_2), 5.12 (1H, br s, 4-H), 5.15 (1H, m, 2β-H), 5.40 (1H, d, J=9 Hz, 3α-H), 5.88 (1H, br s, 22-H).

Preparation of 2α-Acetoxyanhydroperiplogenone (**18**)——A solution of **16** (10 mg) in $CHCl_3$ (2 ml) was stirred with activated MnO_2 (30 mg) at room temperature for 48 h. After removal of the precipitate by filtration, the filtrate was evaporated down. The residue obtained was recrystallized from ether to give **18** (5 mg) as colorless prisms. mp 260—263°C, $[\alpha]_D^{25}$ +38.2° (c=0.17, $CHCl_3$). UV λ_{max}^{MeOH} 235 nm. *Anal.* Calcd for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found: C, 69.97; H, 7.50. ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, s, 18-CH_3), 1.30 (3H, s, 19-CH_3), 2.20 (3H, s, $OCOCH_3$), 4.95 and 5.05 (each 1H, each dd, J=15, 2 Hz, 21-CH_2), 5.40 (1H, dd, J=15, 4 Hz, 2β-H), 5.80 (1H, s, 4-H), 5.90 (1H, br s, 22-H). CD (c=4.331×10^{-4}, MeOH) $[\theta]^{20}$ (nm): −3.694×10^3 (325) (negative max).

Preparation of Desacetylelaeodendrogenin (**21**)——A solution of **16** (12 mg) in MeOH (3 ml) was treated with 5% $KHCO_3$ (2.5 ml), and the mixture was allowed to stand at room temperature for 24 h. The reaction mixture was treated in the usual manner. Recrystallization of the crude product from MeOH gave **21** (5 mg) as colorless prisms. mp 262—266°C, $[\alpha]_D^{20}$ −3.1° (c=0.16, MeOH). *Anal.* Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 70.83; H, 8.37. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, s, 18-CH_3), 1.12 (3H, s, 19-CH_3), 2.80 (1H, br d, J=8 Hz, 17α-H), 3.50 (1H, m, 2β-H), 3.90 (1H, d, J=8 Hz, 3α-H), 4.85 and 5.00 (each 1H, each dd, J=20, 2 Hz, 21-CH_2), 5.10 (1H, br s, 4-H), 5.85 (1H, br s, 22-H).

Preparation of Elaeodendrogenin (**16**)——Anhydroperiplogenone (**19**)[16] (20 mg) obtained from digitoxigenin was treated with $Pb(OAc)_4$ (30 mg) in AcOH (2 ml) at 80°C for 12 h. The reaction mixture was extracted with ether. The organic layer was washed successively with 5% $NaHCO_3$, 5% $NaHSO_3$ and H_2O, dried over anhydrous Na_2SO_4, and evaporated down. The crude 2β-acetoxyanhydroperiplogenone (**20**) was refluxed with AcOK (100 mg) in AcOH (1.5 ml) for 24 h. The reaction mixture was extracted with ether. The organic layer was washed successively with H_2O, 5% $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, and evaporated down. Recrystallization of the crude product from ether gave **18** (3 mg) as colorless prisms. mp 258—260°C. The mixed melting point on admixture with the sample obtained from **16** showed no depression.

A solution of **18** (2 mg) in MeOH (1 ml) was treated with $NaBH_4$ (3 mg), and the solution was allowed to stand at room temperature for 1 h. The reaction mixture was extracted with ether. The organic layer was washed with 5% HCl and H_2O, dried over anhydrous Na_2SO_4, and evaporated down. Recrystallization of the crude product from ether gave **16** (1 mg) as colorless leaflets. mp 257—262°C. The mixed melting point on admixture with the sample obtained from the natural source showed no depression.

Transformation of Elaeodendroside A (**1**) **to Elaeodendroside D** (**3**)——A solution of **1** (100 mg) in MeOH (10 ml) was treated with $NaBH_4$ (20 ml) in H_2O (2 ml) at room temperature for 12 h. The reaction mixture was extracted with AcOEt. The organic layer was washed with 5% HCl and H_2O, dried over anhydrous Na_2SO_4, and evaporated down. The residue obtained was subjected to preparative TLC using benzene–AcOEt (1: 3) as a developing solvent. Elution of the adsorbent corresponding to the desired spot (*Rf* 0.35) with AcOEt and recrystallization of the product from ether–acetone gave 11α,12α-dihydroxyelaeodendroside D (**4**) (70 mg) as a colorless amorphous material. mp 206—210°C, $[\alpha]_D^{21}$ +55.8° (c=0.43, $CHCl_3$). High resolution MS *m/z*: Found: 546.2497. Calcd for $C_{29}H_{38}O_{10}$(M)$^+$=546.2465. Reduction of **2** with $NaBH_4$ in the manner described above gave **4**.

Elution of the adsorbent corresponding to the spot (*Rf* 0.30) with AcOEt and recrystallization of the eluate from CH_2Cl_2–MeOH gave 11α,12β-dihydroxyelaeodendroside D (**5**) (10 mg) as a colorless amorphous material. mp >300°C. $[\alpha]_D^{25}$+30.8° (c=0.13, MeOH–$CHCl_3$ (1: 1)). High resolution MS *m/z*: Found: 546.2485. Calcd for $C_{29}H_{38}O_{10}$(M$^+$)=546.2465. Methanesulfonyl chloride (0.1 ml) was added to a solution of **4** (30 mg) in pyridine (3 ml) under ice-cooling, and the mixture was allowed to stand for 4 h. The reaction mixture was extracted with AcOEt. The organic layer was washed successively with 5% HCl, 5% $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, and evaporated down. NaI (40 mg) and Zn dust (40 mg) were added to a solution of the crude 11α,12α-dihydroxyelaeodendroside D 11-mesylate (**6**) (30 mg) in diglyme (3 ml), and the whole was heated at 80°C for 1 h. The reaction mixture was extracted with AcOEt. The organic layer was washed with 5% $NaHSO_3$ and H_2O, dried over anhydrous Na_2SO_4, and evaporated down. Recrystallization of the crude product from CH_2Cl_2–MeOH gave 12-oxoelaeodendroside D (**7**) (20 mg) as colorless prisms. mp 296—300°C, $[\alpha]_D^{10}$ +135.0° (c=0.10, $CHCl_3$–MeOH (3: 1)). *Anal.* Calcd for $C_{29}H_{36}O_9$:

C, 65.89; H, 6.87. Found: C, 65.92; H, 6.95. ^{1}H-NMR ($CDCl_3$) δ: 1.08 (3H, s, 18-CH_3), 1.22 (3H, s, 19-CH_3), 4.38 (1H, d, J=9 Hz, 3α-H), 4.65 (1H, s, 1'β-H), 4.83 (2H, m, 21-CH_2), 5.15 (2H, ABq, -OCH_2O-), 5.26 (1H, br s, 4-H), 5.95 (1H, br s, 22-H). A solution of **7** (15 mg) in MeOH (5 ml) was refluxed with *p*-tosylhydrazine (20 mg) for 38 h. After removal of the solvent by evaporation, the residue was subjected to preparative TLC using benzene–AcOEt (1: 1) as a developing solvent. Elution of the adsorbent corresponding to the desired spot (*Rf* 0.39) with AcOEt gave the *p*-tosylhydrazone (16 mg) as a colorless amorphous material. A solution of the *p*-tosylhydrazone in dimethylformamide–sulfolane (1: 1) (1 ml) was heated with *p*-toluenesulfonic acid (7 mg) and $NaBH_3CN$ (6 mg) at 105°C for 4 h, then the reaction mixture was extracted with ether. The organic layer was washed with 5% $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, and evaporated down. The residue obtained was subjected to preparative TLC using benzene–AcOEt (1: 1) as a developing solvent. Elution of the adsorbent corresponding to the desired spot (*Rf* 0.30) with AcOEt and recrystallization of the product from CH_2Cl_2–ether gave **3** as colorless leaflets. mp 270—280°C. The mixed melting point on admixture with the sample obtained from the natural source showed no depression.

Transformation of Elaeodendroside H (15) to Elaeodendroside D (3)——A solution of **15** (10 mg) in MeOH (2 ml) was shaken with 5% Pd/C (5 mg) under an H_2 gas stream for 30 min. After removal of the catalyst by filtration, the filtrate was evaporated down. The residue obtained was subjected to preparative TLC using benzene–AcOEt (1: 1) as a developing solvent. Elution of the adsorbent corresponding to the desired spot (*Rf* 0.32) with AcOEt and recrystallization of the product from ether gave **3** (1 mg), which proved to be identical with an authentic sample obtained from the natural source.

Elution of the adsorbent corresponding to the desired spot (*Rf* 0.18) with AcOEt and recrystallization of the product from acetone–ether gave 17α-elaeodendroside D (5 mg) as a colorless amorphous material. mp 254—258°C, $[\alpha]_D^{20}$ +55.8° (c=0.22, $CHCl_3$). High resolution MS m/z: Found: 514.2530. Calcd for $C_{29}H_{38}O_8$(M^+)=514.2565. ^{1}H-NMR ($CDCl_3$) δ: 1.08 (3H, s, 18-CH_3), 1.15 (3H, s, 19-CH_3), 3.19 (1H, t, J= 10 Hz, 17β-H), 4.38 (1H, d, J=10 Hz, 3α-H), 4.65 (1H, s, 1'β-H), 4.75 (2H, m, 21-CH_2), 5.15 (2H, ABq, -OCH_2O-), 5.20 (1H, br s, 4-H), 5.90 (1H, br s, 22-H).

17α-Elaeodendroside D was also obtained from **3** according to the procedure of Merkel *et al.*[12] The two samples were identical with each other.

Chemical Correlation of Elaeodendroside A (1) with Elaeodendroside J (2) and Elaeodendroside I (10)—— Compound **1** (30 mg) was dissolved in MeOH–acetone (1: 1), adsorbed on Al_2O_3 (500 mg), allowed to stand at room temperature for 1 week, and then eluted with CH_2Cl_2–AcOEt (1: 1). The eluate was subjected to preparative TLC using benzene–AcOEt (1: 2) as a developing solvent. Elution of the adsorbent corresponding to the desired spot (*Rf* 0.50) with AcOEt and recrystallization of the product from ether gave **2** as colorless prisms. mp 274—276°C (dec.) The mixed melting point on admixture with an authentic sample showed no depression.

Usual acetylation of **2** (20 mg) with Ac_2O–pyridine followed by recrystallization of the product from acetone–ether gave elaeodendroside J acetate (**12**) (15 mg) as a colorless amorphous material. mp 200—204°C. $[\alpha]_D^{20}$ +22.2° (c=0.09, $CHCl_3$). High resolution MS m/z: Found: 586.2396. Calcd for $C_{31}H_{38}O_{11}$ (M)$^+$=586.2413. Compound **12** was refluxed with Zn dust (100 mg) in AcOH (5 ml)–Ac_2O (0.5 ml) for 3 weeks. The reaction mixture was extracted with AcOEt. The organic layer was washed successively with 5% HCl, 5% $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, and evaporated down. The residue obtained was subjected to preparative TLC using benzene–ether (1: 3) as a developing solvent. Elution of the adsorbent corresponding to the desired spot (*Rf* 0.20) with AcOEt and recrystallization of the product from AcOEt gave 11-oxoelaeodendroside D (**11**) (3 mg) as colorless prisms. mp >300°C. The product proved to be identical with a sample derived from **10** as described below.

Compound **10** (5 mg) was treated with pyridinium chlorochromate (5 mg) under ice-cooling for 4 h. The reaction mixture was extracted with AcOEt. The organic layer was washed with 5% $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, and evaporated down. Recrystallization of the crude product from AcOEt gave **11** (3 mg) as colorless prisms. mp >300°C, $[\alpha]_D^{19}$ +66.7° (c=0.08, $CHCl_3$). High resolution MS m/z: Found: 528.2365. Calcd for $C_{29}H_{36}O_9$ (M)$^+$=528.2359. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, s, 18-CH_3), 1.35 (3H, s, 19-CH_3), 3.60—4.20 (4H, m, 2β-H, 3'α-H, 5'-CH_2), 4.30 (1H, d, J=8 Hz, 3α-H), 4.65 (1H, s, 1'β-H), 4.85 (2H, m, 21-CH_2), 5.15 (2H, ABq, -OCH_2O-), 5.25 (1H, br s, 4-H), 5.90 (1H, br s, 22-H).

Preparation of Elaeodendroside I Acetate (13)——Compound **10** (5 mg) was dissolved in Ac_2O–pyridine (1: 1) (2 ml) and allowed to stand at room temperature for 12 h. After usual work-up, the crude product was recrystallized from acetone to give **13** (2 mg) as colorless prisms. mp >300°C, $[\alpha]_D^{20}$ +15.4° (c=0.07, $CHCl_3$). High resolution MS m/z: Found: 572.2600. Calcd for $C_{31}H_{40}O_{10}$ (M)$^+$=572.2620. ^{1}H-NMR ($CDCl_3$) δ: 1.05 (3H, s, 18-CH_3), 1.20 (3H, s, 19-CH_3), 2.10 (3H, s, $OCOCH_3$), 2.70 (1H, br d, J=8 Hz, 17α-H), 3.50—4.20 (4H, m, 3'α-H, 5'-CH_2, 2β-H), 4.50 (1H, d, J=10 Hz, 3α-H), 4.75 (1H, s, 1'β-H), 4.95 (2H, m, 21-CH_2), 5.10 (1H, m, 11β-H), 5.25 (2H, ABq, -OCH_2O-), 5.35 (1H, br s, 4-H), 5.95 (1H, br s, 22-H).

Structural Elucidation of Elaeodendroside E (8)——Compound **8** (20 mg) in MeOH (1 ml) was added to a solution of $KHCO_3$ (100 mg) in H_2O (2.5 ml) and the mixture was allowed to stand at room temperature for 12 h. The reaction mixture was extracted with AcOEt. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, and evaporated down. Recrystallization of the crude product from ether gave desacetylelaeodendroside E (**9**) (18 mg) as colorless prisms. mp 289—291°C (dec.), $[\alpha]_D^{24.5}$ +34.5° (c=0.17,

$CHCl_3$). *Anal.* Calcd for $C_{29}H_{38}O_9$: C, 65.64; H, 7.22. Found: C, 65.60; H, 7.11. Phenylboric acid (3 mg) was added to a solution of **9** (10 mg) in anhydrous acetone (3 ml), and the mixture was allowed to stand at room temperature for 30 min. After removal of the solvent by evaporation, the residue obtained was subjected to preparative TLC using benzene–AcOEt (4: 1) as a developing solvent. Elution of the adsorbent corresponding to the desired spot (*Rf* 0.38) with AcOEt and recrystallization of the eluate from acetone gave the cyclic phenylboronate (4 mg) as colorless needles. mp 300°C (dec.). MS *m/z*: 616 (M^+), 615.

Compound **8** (10 mg) dissolved in CH_2Cl_2 (1 ml) was adsorbed on Al_2O_3 (200 mg) and dried *in vacuo*. The Al_2O_3 was suspended in benzene (3 ml) and kept at 60°C for 5 h, then eluted with acetone–MeOH. The product was recrystallized from ether to give **15** (2.5 mg) as colorless prisms. mp 293—295°C (dec.). The sample was identical with **15** obtained from the natural source.

Preparation of 11,12-Dioxoelaeodendroside D (14)——Compound **1** (20 mg) in acetone (2 ml) was oxidized with Jones reagent (0.5 ml) under ice-cooling for 10 min. After usual work-up, the crude product was recrystallized from acetone to give **14** (15 mg) as pale yellow crystals. The UV spectrum of this compound suggested the presence of the diosphenol structure. mp 275—280°C, $[\alpha]_D^{25}$ +66.7° (c=0.15, $CHCl_3$–MeOH (1: 1)). MS *m/z*: 542 (M^+). UV λ_{max}^{MeOH} 275 nm.

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