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Novel Diterpenelactones with Anti-peptic Ulcer Activity from *Croton sublyratus*

Eiichi Kitazawa, Aiya Sato, Shuji Takahashi, Harumitsu Kuwano, and Akira Ogiso

Central Research Laboratories, Sankyo Co., Ltd.[1]

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Five novel furanoditerpenes of the *ent*-clerodane type, plaunol A(**1**), B(**2**), C(**3**), D(**4**) and E(**5**), were isolated from a fraction of *Croton sublyratus* Kurz extract with potent anti-Shay ulcer activity. Their absolute structures were determined from the spectral data and by chemical correlations.

Keywords——isolation; structure; *Croton sublyratus*; furanoditerpene; *ent*-clerodane; chemical correlation; anti-Shay ulcer activity

During a continuing search for substances of plant origin with anti-peptic ulcer activity, an acetone extract of stems of *Croton sublyratus* Kurz (Euphorbiaceae) was found to show inhibitory activity against reserpine-induced ulcers in mice and Shay ulcers in rats. Systematic fractionation of the active acetone extract guided by antiulcer activity led to the isolation of 18-hydroxygeranylgeraniol[2] as a principle with anti-reserpine ulcer activity and several furanoditerpenoids as principles with anti-Shay ulcer activity. We report here the structure determination of these furanoditerpenoids.

The acetone extract[2] of the plant furnished, after extensive chromatography, five crystalline lactones designated as plaunol A: $C_{20}H_{20}O_6$ (elemental analysis, mass spectrometry (MS)), mp 214—217°, plaunol B: $C_{20}H_{20}O_6$, mp 184°, plaunol C: $C_{20}H_{20}O_7$, mp 197—199°, plaunol D: $C_{20}H_{22}O_7$, mp 170—172°, and plaunol E: $C_{22}H_{24}O_8$, mp 180—181°. All five compounds were shown to have a β-monosubstituted furan moiety, as indicated by the infrared (IR) absorptions at 3140, 1500 and 870 cm^{-1}, narrow multiplets in the proton magnetic resonance (PMR) spectra at δ 7.4, 7.3 and 6.4, MS fragments at *m/e* 95, 94 and 81 and positive Ehrlich tests. They were also proved to contain an end methylene function by the detection of IR bands at 1640 and 890 cm^{-1} and narrow doublets at δ 5.4—5.0 and 5.2—4.8 in the PMR spectra.

The absolute structure of plaunol A was determined as the structure **1**, an *ent*-clerodane[3] type furanoditerpene, by X-ray analysis of its mono-*p*-bromobenzoate (**6**).[4]

The PMR spectrum of plaunol A (**1**) shows a broad triplet (J=8 Hz, H-12) at δ 5.15 which can be shown to be the X part of an ABX system where A and B (H-11) resonate at δ 2.54 and 2.35, respectively. This triplet is further allylically coupled (J=1 Hz) to a proton on the furan ring (δ 7.58, H-16). Two protons of the end methylene (H-17) show narrow doublets at δ 5.19 and δ 5.24, each of which indicates allylic coupling with the β-proton at C-7 (δ 2.4—2.6, overlapping, J=2 Hz). The doublet at δ 5.47 (J=4.5 Hz, H-19) collapses to a singlet on addition of D_2O due to release of the coupling to a hydroxyl proton (δ 6.11, doublet, J=4.5 Hz). This was confirmed by the observation that this doublet changes to

1) Location: *1-2-58, Hiromachi, Shinagawa-ku, Tokyo.*
2) A. Ogiso, E. Kitazawa, M. Kurabayashi, A. Sato, S. Takahashi, H. Noguchi, H. Kuwano, S. Kobayashi and H. Mishima, *Chem. Pharm. Bull.*, **26**, 3117 (1978).
3) N. Harada and H. Uda, *J. Am. Chem. Soc.*, **100**, 8022 (1978).
4) E. Kitazawa, A. Ogiso, S. Takahashi, A. Sato, M. Kurabayashi, H. Kuwano, T. Hata and C. Tamura, *Tetrahedron Lett.*, **1979**, 1117.

Table I. PMR Spectral Data for Plaunol A–E[11,a]

	Plaunol A (1)	Plaunol B (2)	Plaunol C (3)	Plaunol D (4)	Plaunol E (5)
H-2	*b*)	*b*)	4.80 (m)	4.63 (dd, 11, 2)	4.67 (m)
H-3	6.76 (dd, 4, 3)	6.64 (t, 4)	6.54 (d, 2)	6.61 (d, 2)	6.68 (d, 2.5)
H-6	4.98 (dd, 12, 6)	4.73 (dd, 11, 6)	4.70 (dd, 11, 6.8)	4.68 (dd, 11, 6.5)	4.68 (dd, 11.5, 6.2)
H-7	2.84 (dd, 14, 6)	2.82 (dd, 12.5, 6.5)	2.85 (dd, 12, 6.8)	2.79 (dd, 13, 6.5)	2.83 (dd, 13.5, 6.2)
	2.4—2.6 (ddd, 14, 12, 2)	2.48 (ddd, 12.5, 11, 2)	2.53 (ddd, 12, 11, 2)	2.58 (ddd, 13, 11, 2)	2.45 (ddd, 13.5, 11.5, 2)
H-10	*b*)	*b*)	*b*)	2.38 (m)	2.03 (m)
H-11	2.54 (dd, 13.5, 8)	2.96 (dd, 13.5, 8)	2.95 (dd, 13.5, 8)	2.44 (dd, 15.3, 10)	2.72 (dd, 15.5, 10)
	2.35 (dd, 13.5, 8)	2.56 (dd, 13.5, 8)	2.56 (dd, 13.5, 8)	1.83 (dd, 15.3, 2.8)	1.97 (dd, 15.5, 2)
H-12	5.15 (dt, 1, 8)	5.66 (dt, 1, 8)	5.66 (dt, 1, 8)	4.83 (ddd, 10, 2.8, 1)	5.95 (dd, 10, 2)
H-14	6.52 (m)	6.52 (m)	6.53 (m)	6.41 (m)	6.68 (m)
H-15	7.53 (m)	7.57 (m)	7.58 (m)	7.43 (m)	7.49 (m)
H-16	7.58 (m)	7.66 (m)	7.69 (m)	7.41 (m)	7.49 (m)
H-17	5.24 (d, 2)	5.26 (d, 2)	5.28 (d, 2)	5.32 (d, 2)	5.40 (d, 2)
	5.19 (d, 2)	4.92 (d, 2)	4.94 (d, 2)	4.98 (d, 2)	5.06 (d, 2)
H-19	5.47 (d, 4.5)	3.90 (d, 11)	3.84 (d, 11)	4.02 (d, 11)	4.01 (d, 11)
		3.56 (d, 11)	3.53 (d, 11)	3.27 (dd, 11, 1.5)	3.31 (dd, 11, 1.5)
H-20	5.03 (s)	—	—	4.73 (dd, 4, 2)	4.76 (d, 4)
Misc.	6.11 (d, 4.5, OH-19)	4.0 (br s, OH-19)	4.8 (br s, OH-2)	5.40 (d, 4, OH-20)	5.49 (d, 4, OH-20)
			4.10 (d, 5, OH-19)	4.86 (br s, OH-12)	4.40 (d, 5, OH-2)
				4.2 (br s, OH-2)	2.01 (s, Ac)

a) Run in acetone-d_6 solution. Chemical shifts are in ppm; figures in parentheses are coupling constants in hertz. Abbreviations: s, singlet; d, doublet; t, triplet; br s, broadened singlet; m, multiplet.
b) Could not be identified.

a singlet at δ 6.28 in the PMR spectrum of the monoacetate of **1**. A doublet of doublets at δ 4.98 (J=12 and 6 Hz, H-6) in **1** is the X part of an ABX system where A and B (H-7) resonate at δ 2.4—2.6 (overlapping) and 2.84, respectively. Assignments of the signals of the PMR spectrum of plaunol A, together with those of plaunol B, C, D and E, are shown in Table I.

The spectral properties of plaunol B (**2**) resemble those of **1**. However, the two carbonyl bands absorptions have moved to 1750 and 1725 cm^{-1}, and in the PMR spectrum the singlet due to H-20 of **1** is absent in the case of plaunol B. The signal corresponding to H-12 now appears as a broad triplet (δ 5.66, J=8 Hz), which is the X part of an ABX system with A and B at δ 2.96 and 2.56 (H-11), respectively, and this triplet is further coupled to H-16 (δ 7.66, J=1 Hz) on the furan ring. These observations, together with biogenetic considerations, suggest that the structure of plaunol B contains another saturated lactone ring constructed by linking oxidized C-20 to C-12, the relationship of the furan and lactone moiety being similar to that found in teucvin[5] or bacchotricuneatin B.[6] A doublet at δ 5.47 (H-19) for **1** is replaced by a doublet of doublets of an AB system at δ 3.90 and 3.56 (J=11 Hz), respectively. These signals, changing to a singlet at δ 4.40 in the PMR spectrum of the monoacetate, suggest the presence of a primary hydroxyl group at C-19 in **2**, which was confirmed by the finding that **2** gave an aldehyde (**7**) [δ 9.77 (s, -CHO)] together with a conjugated ketone (**12**)[7] on oxidation with CrO_3/pyridine-water (room temperature, overnight). Based on the above results and comparison of the spectral data for **2** with those for **1**, the structure of

5) E. Fujita, I. Uchida and T. Fujita, *J. Chem. Soc. Perkin Trans. I.*, **1974**, 1547.
6) H. Wagner, R. Seitz, H. Lotter and W. Herz, *J. Org. Chem.*, **43**, 3339 (1978).
7) C.H. Brieskorn and T. Stehle, *Chem. Ber.*, **106**, 922 (1973).

plaunol B was assumed to be **2**. This structure was confirmed by the following chemical conversions.

Reduction of **2** with excess $NaBH_4$ in ethanol (50—55°, 14 hr) gave 3,4-dihydroplaunol B (**8**) and the key intermediate (**9**). This compound (**9**) showed IR bands at 3550, 3380 (hydroxyls) and 1770, 1755 cm^{-1} (saturated γ-lactone). In the PMR spectrum of **9** a triplet

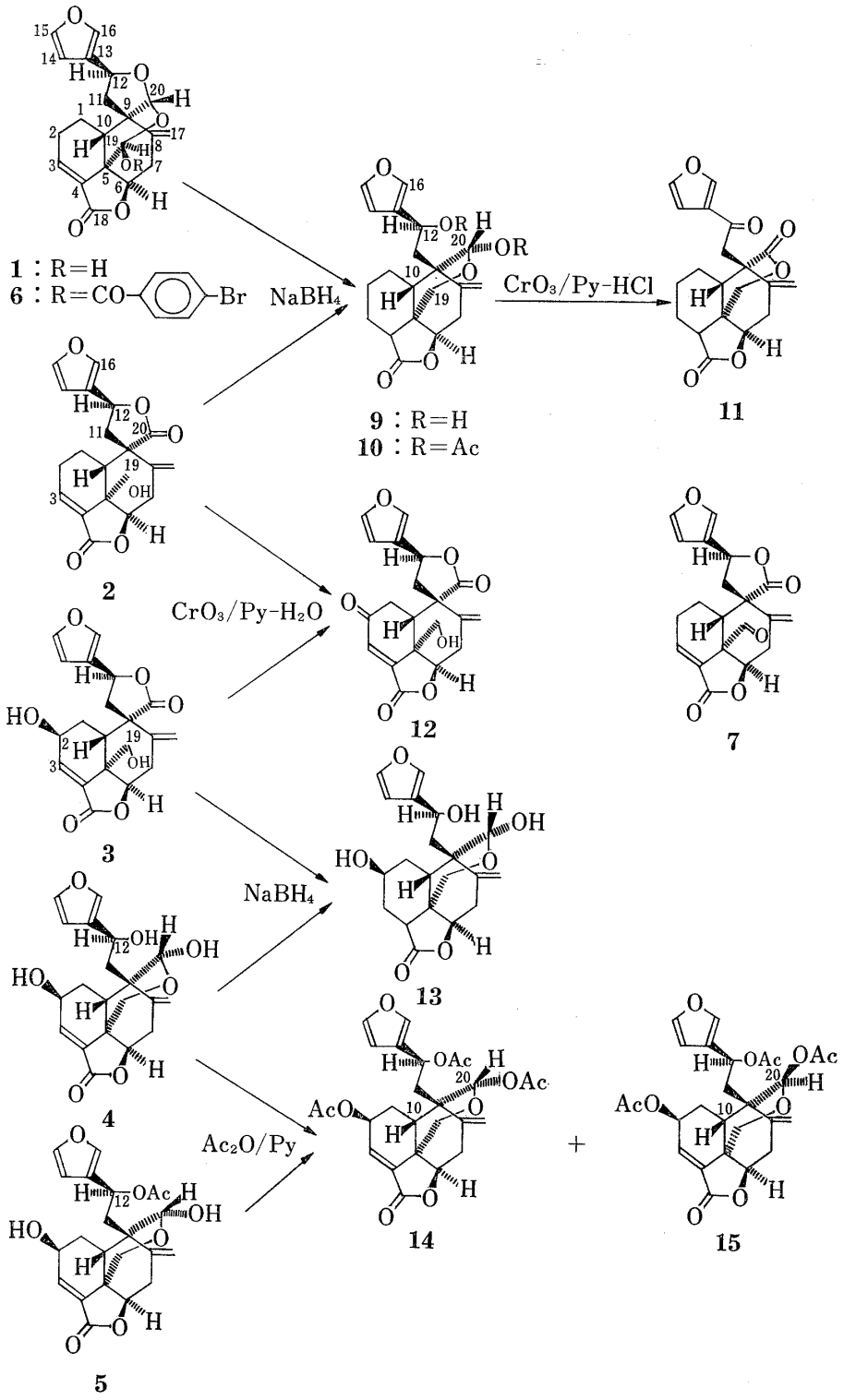

Chart 1

at δ 6.64 (H-3) in **2** shifts upfield and a triplet at δ 5.66 (H-12) also changes to a doublet of doublets at δ 4.82 (J=4.5 and 2.5 Hz), which is assignable to the X part of an ABX system with A and B at δ 2.45 and 1.69, respectively. This signal (H-12), further allylically coupled with a proton on the furan ring (J=1 Hz, H-16), is replaced by a doublet of doublets at δ 6.01 (J=8 and 4 Hz) in the diacetate (**10**). The AB system of H-19 of **9** appears at δ 4.35 and 3.32 (J=11.5 Hz) and the latter is further long-range-coupled with a signal at δ 2.39 (J=1.5 Hz, H-10, W coupling) which is also long-range-coupled to a signal at δ 4.70 (J=1 Hz, H-20, W coupling). The signal due to H-20 shows a doublet of doublets (J=4 and 1 Hz) which changes to a doublet (J=1 Hz) at δ 5.73 in the diacetate (**10**) of **9**, indicating that H-20 couples with the hydroxyl proton on C-20. These assignments were supported by the following results. Oxidation of **9** with pyridinium chlorochromate in methylene chloride (room temperature, overnight) yielded **11**, whose IR spectrum showed the presence of three carbonyl groups, 1765 (γ-lactone), 1730 (δ-lactone) and 1680 cm^{-1} (conjugated ketone). Therefore, one of the two hydroxyl groups of **9** is located at C-12, allylic to the furan ring, and the other is on the hemiacetal structure. The hemiacetal hydroxyl group was concluded to be at C-20, not at C-19, because **9** was obtained under reduction conditions from **2**, bearing the primary hydroxyl group at C-19. This type of reaction with $NaBH_4$ from γ-lactone to δ-lactol has appeared in the literature.[8] The stereochemistry at C-20 was R configuration based on the above-mentioned long-range coupling between H-20 and H-10. Therefore the structure of this key intermediate was assigned as **9**. Furthermore, the absolute configuration of **9** established by a positive Cotton effect (θ^{EtOH}_{231} +10900) in its circular dichroism (CD) spectrum[9] was consistent with that of **6** deduced by X-ray analysis.

On the other hand, reduction of **1** in ethanol with excess $NaBH_4$ (room temperature, overnight) gave 3,4-dihydroplaunol A and **9**, and the latter was identical with the compound obtained from **2** in all physical constants and spectral data. Thus the absolute structure of plaunol B was determined as **2**.

In the PMR spectrum of plaunol C (**3**) a triplet at δ 6.64 (H-3) of **2** changes to a doublet at δ 6.54 (J=2 Hz), which shifts upfield in 3,4-dihydroplaunol C obtained by $NaBH_4$ reduction of **3** in ethanol (room temperature, overnight). However, other signals of **2** and **3** are almost superimposable. Acetylation of **3** gave a diacetate, in the PMR spectrum of which a doublet of doublets of the AB system of **3** at δ 3.84 and 3.53 (J=11 Hz, H-19) changed to a singlet at δ 4.39 and a multiplet at δ 5.87 appeared (H-2). These results and comparison of the molecular formulae of **2** and **3** led to the structure **3** for plaunol C, and this was confirmed by the results of the following chemical conversion. Oxidation of **3** with CrO_3/pyridine–water (room temperature, 5.5 hr) gave **12**, which was identical in all physical constants and spectral data with the ketone obtained from **2** by oxidation with the same reagent (see above). The stereochemistry at C-2 of **3** was proved to be S configuration by the small coupling constant between H-2 and H-3 in the PMR spectrum. The absolute structure of plaunol C is therefore that shown in formula **3**.

The spectral properties of 3,4-dihydroplaunol D (**13**), obtained by reduction of plaunol D (**4**) with excess $NaBH_4$ in ethanol (room temperature, overnight), are fairly similar to those of **9**. Comparing the molecular formula of **13** ($C_{20}H_{24}O_7$) with that of **9** ($C_{20}H_{24}O_6$) and the chemical shift of H-3 in **4** (δ 6.61 doublet, J=2 Hz; this signal shifts upfield in **13**) with that in **3** (δ 6.54, doublet, J=2 Hz), the structure of 3,4-dihydroplaunol D was surmised to be **13**. Reduction of plaunol C with excess $NaBH_4$ in ethanol (55°, 8 hr) gave a triol, which was identical with **13** in all physical constants and spectral data. The absolute structure of 3,4-dihydroplaunol D thus elucidated shows that the structure **4** can be assigned to plaunol D.

Acetylation of **4** with acetic anhydride in pyridine (room temperature, overnight) gave

8) M.L. Wolfrom and H.B. Wood, *J. Am. Chem. Soc.*, 73, 2933 (1951).
9) T. Komori, M. Arita, Y. Ida, T. Fujikura, T. Kawasaki and K. Sekine, *Ann. Chem.*, **1973**, 978.

two isomeric triacetates **14** (amorphous, $[\alpha]_D^{25}$ −50.5°) and **15** (mp 253—255°, $[\alpha]_D^{25}$ −35.2°). They were presumed to be stereoisomeric at C-20 based on the spectral data. The configurations at C-20 of **14** and **15** were clarified to be *S* and *R*, respectively, since long-range coupling (W coupling, J=1 Hz) between H-20 (δ 5.68, doublet) and H-10 was observed in the PMR spectrum of **14**, while in the case of **15** this was not observed. Therefore **15** was considered to be an isomerization product formed under the acetylation conditions.

The spectral properties of plaunol E (**5**) are similar to those of **4**. However, two carbonyl bands are observed at 1750 and 1720 cm^{-1} in the IR spectrum of **5** and in the PMR spectrum of **5** there is a methyl singlet at δ 2.01, representing the acetyl group, and the doublet of doublets at δ 4.83 (H-12) of **4** shifts to a doublet of doublets at δ 5.95 (J=10 and 2 Hz). Based on these findings and comparison of the molecular formula with that of **4**, plaunol E is suggested to be a monoacetate at C-12 of plaunol D. Acetylation of plaunol E with acetic anhydride in pyridine (room temperature, overnight) gave two isomeric triacetates whose physical constants and spectral data were identical with those of **14** and **15**. Thus the absolute structure of plaunol E was assigned as **5**.

Plaunol B, C, D and E exhibited significant inhibitory activity against Shay ulcers in rats[10] (Table II). Several pharmacological tests showed that the activity was caused by the depression of gastric secretion in Shay rats.

Table II. Anti-Shay Ulcer Activity of Plaunol A–E

	Dose (mg/kg, *i.p.*)	No. of rats	% inhibition
Plaunol A	3	5	0
	10	5	0
Plaunol B	3	5	55
	10	5	85
Plaunol C	3	5	36
	10	5	88
Plaunol D	3	5	44
	10	5	61
Plaunol E	3	5	52
	10	5	82

Experimental[11]

Extraction and Isolation of Active Components——Crushed stems of the plant (81.5 kg of a commercial Thai medicinal plant named Plau-noi) were extracted three times with acetone under reflux. After removal of the solvent, the residue was dissolved in 10 l of 80% aqueous methanol and washed with *n*-hexane. The concentrated methanol layer was poured into 40 l of benzene with vigorous stirring. After washing with aqueous sodium hydrogen carbonate, the benzene solution was evaporated and the residue was extracted with ether. From the ether–soluble fraction, 18-hydroxygeranylgeraniol was isolated.[2] The ether–insoluble fraction was chromatographed on silica gel (5 kg), eluting with chloroform and methanol. Repeated chromatography on silica gel, eluting with benzene and ethyl acetate, gave five furanoditerpenoids, plaunol A (**1**) (yield 5.6 g), B (**2**) (1.2 g), C (**3**) (1.5 g), D (**4**) (0.5 g) and E (**5**) (4.1 g).

Plaunol A: mp 214—217°, $[\alpha]_D^{23}$ −61.7° (c=1.0, acetone). IR ν_{max}^{Nujol} cm^{-1}: 3400, 3150, 1735, 1725, 1675, 1645, 1505, 885, 878. MS *m/e*: 356 (M^+), 338, 311, 281, 263, 237, 213, 187, 135, 110, 95, 94, 81 (base). *Anal.* Calcd for $C_{20}H_{20}O_6$: C, 67.41; H, 5.66. Found: C, 67.74; H, 5.59.

10) H. Shay, S.A. Komarov, S.S. Fels, D. Meranze, M. Gluenstein and H. Siplet, *Gastroenterology*, **5**, 43 (1945).

11) The PMR spectra were measured with Varian T-60 and HA-100 spectrometers using tetramethylsilane as an internal standard. The IR spectra were determined with a JASCO IRA-2 spectrophotometer. The MS spectra were measured with a JEOL JMS-01SG spectrometer. Preparative thin–layer chromatography was performed using Silica gel 60 F_{254} TLC plates (thickness 2 mm, E. Merck). For column chromatography, silica gel 60—110 mesh (Kanto Chemical Co., Inc., Tokyo) was used. Anti-Shay ulcer activity was tested in rats by the reported method.[2,10]

Plaunol B: mp 184°, $[\alpha]_D^{24}$ +41.4° (c=0.35, acetone). IR ν_{max}^{Nujol} cm^{-1}: 3340, 3140, 1750, 1725, 1665, 1635, 1505, 895, 878. MS m/e: 356 (M$^+$), 338, 326, 311, 310, 281, 232, 129, 95 (base), 94, 81. *Anal.* Calcd for $C_{20}H_{20}O_6$: C, 67.41; H, 5.66. Found: C, 67.27; H, 5.66.

Plaunol C: mp 197—199°, $[\alpha]_D^{24}$ −13.0° (c=1.28, acetone). IR ν_{max}^{Nujol} cm^{-1}: 3400, 3150, 1770, 1720, 1705, 1660, 1640, 1505, 890, 875. MS m/e: 372 (M$^+$), 354, 336, 326, 296, 222, 130, 128, 114, 95 (base), 94, 81. *Anal.* Calcd for $C_{20}H_{20}O_7$: C, 64.51; H, 5.41. Found: C, 64.17; H, 5.43.

Plaunol D[12]: mp 170—172°, $[\alpha]_D^{20}$ −144° (c=1.0, acetone). IR ν_{max}^{Nujol} cm^{-1}: 3450, 3320, 3160, 1740, 1680, 1640, 1600, 1505, 890, 875. MS m/e: 374 (M$^+$), 356, 338, 311, 288, 232, 214, 157, 97, 95, 94, 81. *Anal.* Calcd for $C_{20}H_{22}O_7$: C, 64.16; H, 5.92. Found: C, 63.93; H, 6.00.

Plaunol E[12]: mp 180—181°, $[\alpha]_D^{20}$ −142° (c=1.0, acetone). IR ν_{max}^{Nujol} cm^{-1}: 3380, 3160, 1750, 1720, 1675, 1635, 1505, 895, 875. MS m/e: 416 (M$^+$), 398, 356, 338, 279, 278, 250, 232, 214, 139, 97, 95, 94, 81. *Anal.* Calcd for $C_{22}H_{24}O_8$: C, 63.45; H, 5.81. Found: C, 63.54; H, 5.78.

Plaunol A (1) Mono-*p*-bromobenzoate——To a solution of 99 mg of plaunol A in 5 ml of pyridine was added 0.2 g of *p*-bromobenzoyl chloride at 0°, and the mixture was allowed to stand overnight at room temperature. The reaction mixture was poured into ice-water and extracted with chloroform. The chloroform layer was washed with water. Removal of the solvent and recrystallization of the residue from methylene chloride-ligroin gave 119 mg of the desired crystals of mono-*p*-bromobenzoate (**6**), mp 203—204°, $[\alpha]_D^{24}$ −115.8° (c=1.0, acetone). IR ν_{max}^{KBr} cm^{-1}: 3140, 1765, 1735, 1675, 1640, 1590, 1505, 1485, 1265, 1220, 1065. PMR (acetone-d_6) δ: 7.93 (2H, d, J=9 Hz), 7.72 (2H, d, J=9 Hz), 7.63 (1H, m), 7.54 (1H, m), 6.89 (1H, dd, J=4, 3 Hz), 6.56 (1H, m), 6.49 (1H, br s), 5.29 (1H, d, J=2 Hz), 5.27 (1H, d, J=2 Hz), 5.25 (1H, m), 5.23 (1H, dd, J=12, 6 Hz), 5.16 (1H, br s), 3.1—2.1 (9H). MS m/e: 540, 538 (M$^+$), 493, 491, 338, 309, 291, 281, 280, 185, 183, 156, 154, 95, 94, 81. *Anal.* Calcd for $C_{27}H_{23}O_7Br$: C, 60.12; H, 4.30; Br, 14.81. Found: C, 59.95; H, 4.23; Br, 14.98.

Plaunol A (1) Monoacetate——A solution of 100 mg of **1** in 1 ml of pyridine and 0.3 ml of acetic anhydride was allowed to stand overnight at room temperature. The reaction mixture was treated as described for the synthesis of **6**. The crude products were purified by column chromatography on silica gel, eluting with benzene–ethyl acetate (2: 1) to give 65 mg of the monoacetate of **1**: mp 185—187°. IR ν_{max}^{Nujol} cm^{-1}: 3140, 1760, 1670, 1640, 1503, 1225, 1145, 1060, 1030, 1000, 903, 880. PMR (acetone-d_6) δ: 7.57 (2H, m), 6.90 (1H, m), 6.58 (1H, m), 6.28 (1H, s), 5.32 (1H, m), 5.30 (1H, s), 5.26 (1H, br s), 5.08 (1H, br s), 5.02 (1H, dd, J=11.5, 6 Hz), 2.03 (3H, s), 2.9—2.1 (9 H). MS m/e: 398 (M$^+$), 353, 320, 310 (base), 292, 281, 265, 149, 95, 94, 81. *Anal.* Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57. Found: C, 66.29; H, 5.47.

$NaBH_4$ Reduction of Plaunol A (1)——To a solution of 100 mg of **1** in 10 ml of ethanol was added 37 mg of $NaBH_4$ and the mixture was stirred overnight at room temperature. After quenching the reaction with acetic acid and removing the solvent, the residue was purified by chromatography on silica gel, eluting with benzene–ethyl acetate (2: 1) to give 14 mg of 3,4-dihydroplaunol A: mp 163—164°. IR ν_{max}^{Nujol} cm^{-1}: 3340, 3120, 1790, 1645, 1500, 1305, 1150, 1115, 1020, 935, 910, 870. PMR ($CDCl_3$) δ: 7.36 (2H, m), 6.33 (1H, m), 5.73 (1H, s), 5.28 (1H, s), 5.08 (1H, t, J=7 Hz), 4.87 (1H, m), 4.82 (1H, dd, J=10, 7 Hz), 4.75 (1H, m), 3.0—1.5 (13H). MS m/e: 358 (M$^+$), 340, 312, 237, 169, 95, 94, 81 and 57 mg of **9**: mp 180°, $[\alpha]_D^{23}$ −109° (c=0.97, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3530, 3350, 3140, 1770, 1755, 1640, 1503, 995, 875. PMR (acetone-d_6) δ: 7.40 (2H, m), 6.40 (1H, m), 5.32 (1H, d, J=4 Hz), 5.15 (1H, m), 4.84 (1H, m), 4.82 (1H, m), 4.70 (1H, dd, J=4, 1 Hz), 4.54 (1H, dd, J=8, 7 Hz), 4.35 (1H, d, J=11.5 Hz), 3.32 (1H, dd, J=11.5, 1.5 Hz), 3.02 (1H, dd, J=16, 8 Hz), 2.85—1.4 (12H). MS m/e: 360 (M$^+$), 342, 324, 296, 283, 218, 173, 159, 97 (base), 95, 94, 81. *Anal.* Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.44; H, 6.86. CD curve (EtOH) $[\theta]_{300}$ 0, $[\theta]_{231}$ +10900, $[\theta]_{229}$ +4100 (last reading).

Compound (9) Diacetate——A solution of 20 mg of compound (**9**) in 1 ml of pyridine and 0.5 ml of acetic anhydride was allowed to stand overnight at room temperature. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The ethyl acetate layer was washed with water and concentrated to give 20 mg of the desired diacetate as an amorphous solid. IR ν_{max}^{Nujol} cm^{-1}: 3030, 1770, 1742, 1635, 1503, 1320, 1225, 1165, 1065, 995, 870. PMR ($CDCl_3$) δ: 7.31 (2H, m), 6.30 (1H, m), 5.91 (1H, dd, J=8, 4 Hz), 5.73 (1H, s), 5.30 (1H, br s), 5.10 (1H, br s), 4.50 (1H, t, J=8 Hz), 4.14 (1H, d, J=12 Hz), 3.62 (1H, d, J=12 Hz), 2.03 (3H, s), 1.93 (3H, s), 3.3—1.2 (12H). MS m/e: 444 (M$^+$), 402, 384, 342, 324, 296, 237, 97, 95, 81.

Oxidation of Compound (9)——To a solution of 40 mg of compound (**9**) in 5 ml of methylene chloride was added 35 mg of pyridinium chlorochromate, and the mixture was allowed to stand for 3 hr at room temperature. After adding 15 ml of ethyl acetate, the mixture was filtered and the filtrate was evaporated to dryness. The residue was purified by preparative thin-layer chromatography on silica gel, developing with benzene–ethyl acetate (3: 2) to give 15 mg of compound (**11**): mp 163°. IR ν_{max}^{KBr} cm^{-1}: 3130, 2910, 1765, 1730, 1680, 1640, 1560, 1505, 1190, 1150, 995, 890. PMR (acetone-d_6) δ: 8.47 (1H, m), 7.60 (1H, m), 6.77 (1H, m), 5.13 (2H, m), 4.65 (1H, d, J=12.5 Hz), 4.64 (1H, dd, J=12, 6 Hz), 4.39 (1H, d, J=12.5 Hz),

12) Physical and spectral data for plaunol D and E correspond to those of furanoditerpene B and A, respectively, in the previous report.[2]

3.62 (1H, d, J=18 Hz), 3.42 (1H, d, J=18 Hz), 3.05—1.2 (10H). MS *m/e*: 356 (M^+), 328, 312, 262, 172, 95.

Plaunol B (2) Monoacetate——A solution of 70 mg of plaunol B in 1 ml of pyridine and 0.5 ml of acetic anhydride was allowed to stand overnight at room temperature. Usual work-up gave 47 mg of the desired monoacetate as an amorphous solid. IR ν_{max}^{Nujol} cm^{-1}: 3120, 1760, 1740, 1665, 1640, 1230, 1180, 1035, 910, 875. PMR ($CDCl_3$) δ: 7.53 (2H, m), 6.84 (1H, t, J=4 Hz), 6.44 (1H, m), 5.58 (1H, t, J=8 Hz), 5.32 (1H, m), 5.02 (1H, m), 4.67 (1H, dd, J=11.5, 7 Hz), 4.40 (2H, s), 1.94 (3H, s), 3.1—1.9 (9H). MS *m/e*: 398 (M^+), 380, 356, 338, 320, 308 (base), 270, 263, 213, 95, 94, 81. *Anal.* Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57. Found: C, 66.04; H, 5.68.

Oxidation of Plaunol B (2)——Plaunol B (100 mg) was added to a solution of 100 mg of CrO_3 in 10 ml of pyridine containing 1 drop of water, and the mixture was stirred overnight. After filtration ethyl acetate was added to the filtrate. The ethyl acetate layer was washed with water. Upon concentration and purification by preparative thin-layer chromatography, 9 mg of an aldehyde (**7**) and 21 mg of a conjugated ketone (**12**) were obtained and 25 mg of unreacted plaunol B was recovered. **7**: PMR ($CDCl_3$) δ: 9.77 (1H, s), 7.53 (2H, m), 7.10 (1H, m), 6.48 (1H, m), 5.59 (1H, t, J=9 Hz), 5.40 (1H, m), 5.17 (1H, dd, J=12, 7 Hz), 5.08 (1H, br s), 3.1—1.9 (9H). **12**: mp 124—126°, $[\alpha]_D^{23}$ −36.1° (c=1.0, acetone). IR ν_{max}^{Nujol} cm^{-1}: 3450, 3150, 1770, 1695, 1645, 1505, 995, 878. PMR ($CDCl_3$) δ: 7.78 (1H, m), 7.67 (1H, m), 6.63 (1H, m), 6.49 (1H, s), 5.78 (1H, t, J=8.5 Hz), 5.45 (1H, m), 5.07 (1H, br s), 4.80 (1H, dd, J=12, 7 Hz), 4.02 (2H, m), 3.4—2.3 (8H). MS *m/e*: 370 (M^+), 352, 340, 295, 246, 148, 115, 95, 94, 81. *Anal.* Calcd for $C_{20}H_{18}O_7$: C, 64.86; H, 4.90. Found: C, 64.59; H, 4.99.

$NaBH_4$ Reduction of Plaunol B (2)——To a solution of 100 mg of plaunol B (**2**) in 10 ml of ethanol was added 40 mg of $NaBH_4$ and the mixture was stirred for 55 hr at 50—55°. Work-up as described after the reduction of **1** gave 37 mg of 3,4-dihydroplaunol B, mp 127°. IR ν_{max}^{Nujol} cm^{-1}: 3440, 1760, 1640, 1505, 1165, 1125, 1010, 965, 885. PMR (acetone-d_6) δ: 7.63 (2H, m), 6.51 (1H, m), 5.70 (1H, dd, J=9, 6 Hz), 5.02 (1H, m), 4.80 (1H, m), 4.71 (1H, dd, J=10, 7 Hz), 3.88 (2H, m), 3.25—1.4 (13H). MS *m/e*: 358 (M^+), 340, 312, 282, 144, 95, 94, 81. In addition, 30 mg of a diol identical with **9** obtained from **1** was isolated.

Plaunol C (3) Diacetate——A solution of 150 mg of plaunol C (**3**) in 3 ml of pyridine and 0.5 ml of acetic anhydride was allowed to stand overnight at room temperature. Usual work-up gave 101 mg of the desired diacetate, IR ν_{max}^{Nujol} cm^{-1}: 3140, 1770, 1750, 1640, 1505, 1250, 1210, 1095, 1030, 885. PMR (acetone-d_6) δ: 7.17 (2H, m), 6.69 (1H, d, J=1.5 Hz), 6.59 (1H, m), 5.87 (1H, dd, J=5, 1.5 Hz), 5.71 (1H, t, J=9 Hz), 5.38 (1H, m), 5.06 (1H, m), 4.65 (1H, dd, J=11.5, 6.5 Hz), 4.39 (1H, s), 2.09 (3H, s), 1.96 (3H, s), 3.3—2.1 (8H).

Oxidation of Plaunol C (3)——Plaunol C (100 mg) was added to a solution of 100 mg of CrO_3 in 1 ml of pyridine containing 1 drop of water, and the reaction mixture was stirred overnight at room temperature. Work-up as described after the oxidation of plaunol B gave 79 mg of the desired conjugated ketone, which was identical with **12** obtained from **2**.

$NaBH_4$ Reduction of Plaunol C (3)——(a) To a solution of 100 mg of plaunol C (**3**) in 10 ml of ethanol was added 20 mg of $NaBH_4$ and the mixture was stirred overnight at room temperature. Usual work-up gave 75 mg of 3,4-dihydroplaunol C, IR ν_{max}^{Nujol} cm^{-1}: 3520, 3400, 1780, 1770, 1650, 1190, 1170, 1095, 1015, 885. PMR (acetone-d_6) δ: 7.69 (1H, m), 7.63 (1H, m), 6.56 (1H, m), 5.72 (1H, dd, J=9, 6 Hz), 5.13 (1H, d, J=2 Hz), 4.80 (1H, d, J=2 Hz), 4.71 (1H, dd, J=9, 7 Hz), 4.18 (2H, m), 3.90 (2H, m), 3.58 (1H, m), 3.25—1.6 (10H).

(b) To a solution of 100 mg of plaunol C (**3**) in 10 ml of ethanol was added 35 mg of $NaBH_4$, and the mixture was stirred for 8 hr at 55°. Work-up as described in (a) gave 35 mg of 3,4-dihydroplaunol C and 8 mg of **13**, mp 120—122°, $[\alpha]_D^{24}$ −81.2° (c=0.2, acetone). IR ν_{max}^{KBr} cm^{-1}: 3420, 2930, 1760, 1635, 1500, 1185, 1150, 1100, 1085, 875. PMR (acetone-d_6) δ: 7.39 (2H, m), 6.39 (1H, m), 5.16 (1H, d, J=4 Hz), 5.12 (1H, m), 4.82 (1H, d, J=3 Hz), 4.71 (1H, m), 4.49 (1H, dd, J=9, 8 Hz), 4.30 (1H, d, J=11 Hz), 4.10 (2H, m), 3.72 (1H, dd, J=14, 9 Hz), 3.30 (1H, dd, J=11, 2 Hz), 3.1—1.5 (11H). MS *m/e*: 376 (M^+), 358, 340, 312, 281, 280, 157, 97, 95, 94, 81. *Anal.* Calcd for $C_{20}H_{24}O_7$: C, 63.82; H, 6.43. Found: C, 63.55; H, 6.61.

$NaBH_4$ Reduction of Plaunol D (4)——To a solution of 100 mg of plaunol D (**4**) in 15 ml of ethanol was added 10 mg of $NaBH_4$, and the mixture was stirred overnight at room temperature. Work-up as described after the reduction of **3** gave 47 mg of 3,4-dihydroplaunol D whose physical constants and spectral data were identical with those of **13** obtained from **3**.

Acetylation of Plaunol D (4)——A solution of 100 mg of plaunol D (**4**) in 2 ml of pyridine and 0.5 ml of acetic anhydride was allowed to stand overnight at room temperature. Usual work-up and recrystallization from ethyl acetate gave 30 mg of crystalline **15**. The mother liquor was purified by preparative thin-layer chromatography on silica gel, developing with benzene–ethyl acetate (2: 1) to give 25 mg of **14** as an amorphous solid, $[\alpha]_D^{25}$ −50.5° (c=0.43, acetone). IR ν_{max}^{Nujol} cm^{-1}: 3150, 1765, 1743, 1680, 1640, 1600, 1505, 1230, 1180, 1100, 1025, 990, 870. PMR (acetone-d_6) δ: 7.52 (1H, m), 7.47 (1H, m), 6.62 (1H, d, J=2.5 Hz), 6.44 (1H, m), 5.99 (1H, m), 5.74 (1H, m), 5.68 (1H, d, J=1 Hz), 5.53 (1H, d, J=2.5 Hz), 5.25 (1H, d, J=2.5 Hz), 4.72 (1H, dd, J=11.5, 6.5 Hz), 4.00 (1H, d, J=11.5 Hz), 3.57 (1H, dd, J=11.5, 1 Hz), 2.16 (3H, s), 2.08 (3H, s), 2.06 (3H, s), 3.1—2.3 (7H). MS *m/e*: 500 (M^+), 458, 440, 398, 380, 338, 322, 292, 279, 211, 167, 97, 95, 81. *Anal.* Calcd for $C_{26}H_{28}O_{10}$: C, 62.39; H, 5.64. Found: C, 62.45; H, 5.56. The isomer **15**, mp 253—255°, $[\alpha]_D^{25}$ −35.2° (c=0.35, acetone). IR ν_{max}^{Nujol} cm^{-1}: 3150, 1765, 1750, 1730, 1678, 1640, 1605,

1503, 1230, 1218, 1160, 1060, 1025, 975, 910, 875. PMR (acetone-d_6) δ: 7.52 (1H, m), 7.46 (1H, m), 6.62 (1H, d, J=2.5 Hz), 6.44 (1H, m), 6.01 (1H, m), 5.82 (1H, s), 5.79 (1H, m), 5.49 (1H, dd, J=2.5, 1 Hz), 5.30 (1H, dd, J=2.5, 1 Hz), 4.73 (1H, dd, J=11.5, 7 Hz), 4.00 (1H, d, J=11.5 Hz), 3.70 (1H, dd, J=11.5, 1.5 Hz), 2.08 (3H, s), 2.06 (3H, s), 2.02 (3H, s), 3.1—2.1 (7H). *Anal.* Calcd for $C_{26}H_{28}O_{10}$: C, 62.39; H, 5.64. Found: C, 62.51; H, 5.55.

Acetylation of Plaunol E (5)——Plaunol E (**5**) (50 mg) was acetylated under the same conditions as **4** to give 19 mg of **14** and 15 mg of **15**, which were identical with the triacetates obtained from **4**.

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