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NEW CYTOTOXIC NOR- AND BISNORDITERPENE DILACTONES, MAKILACTONES A-D, FROM *PODOCARPUS MACROPHYLLUS* D. DON

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Abstract – Four new nor- and bisnorditerpene dilactones, makilactones A-D, were isolated from a MeOH extract of bark and root of *Podocarpus macrophyllus* D. Don（Podocarpaceae) with three known diterpene dilactones. The structures of the new nor- and bisnorditerpene dilactones having a 7:8, 9:11-dienolide moiety were determined by the spectroscopic studies, including 1D and 2D NMR spectral analysis, and single crystal X-Ray crystallographic analysis. Two of the presently isolated compounds were shown to be very strongly cytotoxic.

INTRODUCTION

Podocarpus macrophyllus D. Don (Podocarpaceae) (Japanese name: *Inumaki*) is a dioecious evergreen tree distributed in the subtropical areas of south eastern China, Taiwan, and Japan. From this plant, flavonoids, bisflavonoids, ecdysons, norditerpenoids,[1-4] and antibiotic diterpenes have been reported.[5] From a related *Podocarpus* plant, *Podocarpus macrophyllus* D. Don var. *maki*, nor- and bisnorditerpenoids having cytotoxic activities against P388 murine leukemia cells have also been reported by us.[6-8]

In the present study, from the bark and root of *Podocarpus macrophyllus* D. Don, we further isolated four new nor- and bisnorditerpene dilactones, makilactones A-D, along with three known norditerpene dilactones, nagilctone F, 2α-hydroxynagilactone F and 3β-hydroxynagilactone F, and determined the structures of the new diterpene dilactones mainly on the basis of the spectroscopic studies including

X-ray crystallography. All the present diterpenoids were shown to have a 7:8, 9:11-dienolide moiety, which is considered to be associated with cytotoxic activity.

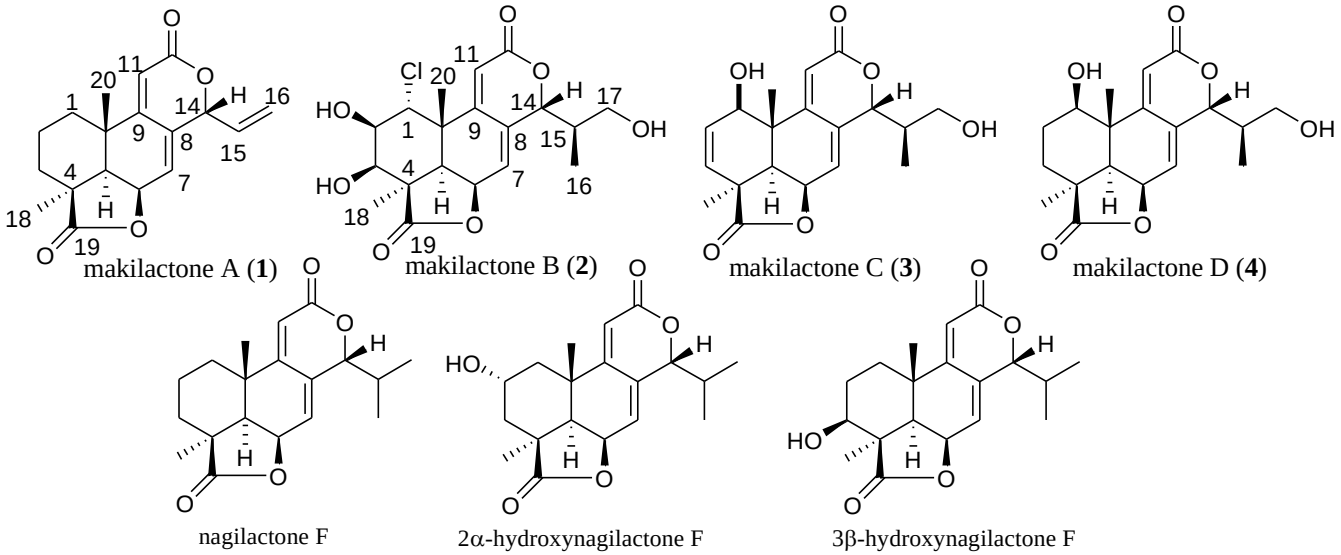

Figure 1. Bisnor- and nor diterpene dilactones isolated from *Podocarpus macrophyllus* D Don.

ESULTS AND DISCUSSION

Makilactone A (**1**) was isolated as colorless needles, mp 236-239℃. The molecular formula was determined to be $C_{18}H_{20}O_4$ from the [M^++H] ion peak at *m/z* 301.1444 in HRESIMS. IR absorption bands at 1702 cm^{-1} and 1769 cm^{-1} indicated the presence of γ-lactone carbonyl and δ-lactone carbonyl groups. The profiles of the NMR spectra of **1** and nagilactone F, a known norditerpene dilactone also isolated in the present study, were generally quite similar to each other, as shown in Table 1. In the HMQC spectrum, the two methyl carbon signals at δ_C 24.0 and δ_C 24.3 correlated with the proton signals at δ_H 1.23 and δ_H 1.07, respectively, and were assigned to C-18 methyl and C-20 methyl, respectively. The fact implied that they had the same basic carbon skeleton structure with a 7:8, 9:11-dienolide unit (hereafter, the carbon skeleton structure without the C-14 side chain will be referred to as nagilactone F unit). The difference between **1** and nagilactone F was only in the C-14 side chain structure. The carbon signals in the lower magnetic field at δ_C 132.8 and δ_C 122.0 were assigned to C-15 and C-16, forming a vinyl group in the side chain. Thus, the structure of **1** was determined to be as shown in Figure 1. The ORTEP representation derived from the X-ray crystallographic analysis

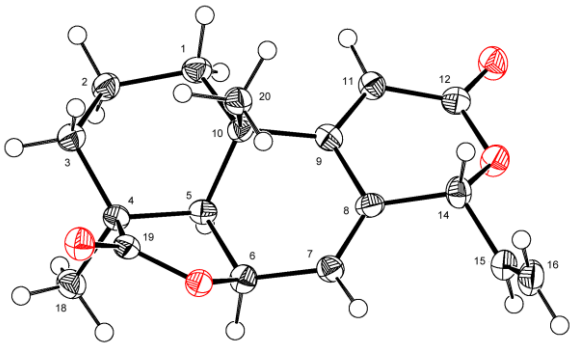

Figure 2. ORTEP representation of **1** as determined by single crystal X-ray crystallographic analysis.

Table 1. ^{13}C-NMR Data of makilactones A-D (**1** – **4**) and nagilactone F in pyridine-d_5.

	makilactone A (**1**)[b]	makilactone B (**2**)[a]	makilactone C (**3**)[a]	makilactone D (**4**)[a]	nagilactone F[b]
1	29.8	65.5	70.2	69.4	30.0
2	17.6	74.3	135.2	29.8	17.7
3	28.0	72.2	127.6	27.5	28.0
4	42.9	45.9	44.9	42.9	42.9
5	47.4	43.9	47.0	47.3	47.0
6	71.8	71.8	71.1	72.2	72.1
7	122.0	122.0	122.2	122.5	122.5
8	135.0	134.2	134.8	134.4	134.0
9	158.8	155.0	156.9	158.4	159.2
10	35.1	42.4	40.2	40.6	35.0
11	112.2	115.4	115.2	114.7	112.3
12	163.7	163.8	164.5	164.6	164.1
14	80.6	81.9	81.9	81.9	82.9
15	132.8	40.5	37.8	38.0	29.5
16	122.0	14.7	15.4	15.3	15.3
17		62.2	62.5	62.5	19.7
18	24.0	23.1	23.1	23.9	24.1
19	181.1	178.4	178.1	181.1	181.1
20	24.3	26.8	15.8	17.2	24.7

a) Recorded at 125 MHz. *b*) Recorded at 150 MHz.

Table 2. ^{1}H- NMR Data of makilactones A-D (**1** – **4**) and nagilactone F in pyridine-d_5.

	makilactone A (**1**)[b]	makilactone B (**2**)[a]	makilactone C (**3**)[a]	makilactone D (**4**)[a]	nagilactone F[b]
1	1.36 (1H, m)	5.01(1H, d, 3.9)	4.66 (1H, d, 6.2)	4.10 (1H, br dd)	1.34 (1H, m)
	1.47 (1H, m)				1.47 (1H, m)
2	1.43 (1H, m)	4.71 (1H, br m)	6.00 (1H, dd, 10.1, 0.8)	1.94 (1H, m)	1.44 (1H, m)
	1.61 (1H, m)			2.00 (1H, m)	1.61 (1H, m)
3	1.39 (1H, m)	4.40 (1H, br m)	5.96 (1H, dd, 10.1, 1.9)	1.53 (1H, m)	1.39 (1H, m)
	2.19 (1H, m)			2.48 (1H, m)	2.21 (1H, m)
5	1.67 (1H, d, 4.8)	2.72 (1H, d, 4.5)	2.14 (1H, d, 5.0)	1.78 (1H, d, 4.8)	1.67 (1H, d, 4.9)
6	5.00 (1H, dd, 4.8, 4.8)	5.24 (1H, dd, 5.6, 5.6)	5.14 (1H, m)	5.08 (1H, dd, 4.7, 4.7)	5.09 (1H, d, m)
7	6.15 (1H, m)	6.50 (1H, m)	6.55 (1H, m)	6.52 (1H, m)	6.23 (1H, m)
11	5.89 (1H, d, 1.5)	6.41 (1H, d, 1.9)	6.96 (1H, d, 1.6)	6.87 (1H, s)	5.88 (1H, 1.9)
14	5.48 (1H, m)	5.31 (1H, m)	5.14 (1H, m)	5.11 (1H, br m)	4.84 (1H, m)
15	6.05 (1H, ddd, 17.2, 10.3, 7.6)	2.55 (1H, m)	2.62 (1H, m)	2.60 (1H, m)	2.19 (1H, m)
16	5.43 (1H, d, 10.3)	1.30 (3H, d, 6.9)	1.42 (3H, d, 6.8)	1.40 (3H, d, 6.8)	0.97 (3H, d, 6.9)
	5.48 (1H, dd, 17.2, 1.0)				
17		3.89 (1H, br dd)	3.95 (1H, m)	3.94 (1H, br dd)	1.12 (3H, d, 6.8)
		4.05 (1H, br dd)	4.20 (1H, ddd, 10.7, 4.4, 4.4)	4.18 (1H, br dd)	
18	1.23 (3H, s)	1.66 (3H, s)	1.37 (3H, s)	1.26 (3H, s)	1.25 (3H, s)
20	1.07 (3H, s)	1.99 (3H, s)	1.45 (3H, s)	1.45 (3H, s)	1.09 (3H, s)
OH-1			7.21 (1H, d, 6.6)	6.70 (1H, br d)	
OH-2		8.17 (1H, br d)			
OH-3		5.95 (1H, br d)			
OH-17		6.34 (1H, br d)	6.28 (1H, br t)	6.29 (1H, br t)	

a) Recorded at 500 MHz. *b*) Recorded at 600 MHz.

is shown in Figure 2.

Makilactone B (**2**) was isolated as colorless needles, mp 218℃. The molecular formula was determined to be $C_{19}H_{23}O_7Cl$ from the $[M^+ + Na]$ ion peak at *m/z* 421.1017 in HRESIMS. The presence of a chlorine atom in **2**, was implied by the ESIMS, by the $[M + Na]^+$ ion peak at 421.1017 and the chlorine isotope (^{37}Cl) peak at 423.1029. IR absorptions bands at 1774 cm^{-1}, 1693 cm^{-1} and 3311 cm^{-1} showed the presence of γ-lactone carbonyl, δ-lactone carbonyl and hydroxyl groups, respectively. The ^{13}C and ^1H NMR spectra of **2** showed that it had three methyls and three hydroxyls, and that it had the nagilactone F unit as **1**, in which two of the three methyl carbon signals at δ_C 23.1 and δ_C 26.8 correlating with the singlet methyl proton signals at δ_H 1.66 and δ_H 1.99, respectively in the HMQC spectrum were assigned to C-18 methyl and C-20 methyl, respectively. The other methyl carbon signal at δ_C 14.7 correlating with the doublet methyl proton signal at δ_H 1.30 in the HMQC spectrum was assigned to C-16 methyl of the side chain. In the COSY spectrum, the methylene proton signals H-17 (δ_H 3.89 and δ_H 4.05) were both correlated with the hydroxyl group at δ_H 6.34, which implied that a hydroxyl methyl group was connected to C-15. In the COSY spectrum, the proton signals of H-2 (δ_H 4.71) and of H-3 (δ_H 4.40) correlated with the hydroxyl protons at δ_H 8.17 and at δ_H 5.95, respectively, to show that the remaining two hydroxyls were at C-2 and C-3. The HMBC correlations were observed between H-14 and the carbons C-8, C-7, and C-16, which indicated the presence of 2-hydroxy-1-methylethan-2-yl substituent at C-14 (Figure 3a). In the NOESY spectrum, the proton signal H-1 (δ_H 5.01) was correlated with the methyl proton signal H-20 (δ_H 1.99), the proton signal H-2 (δ_H 4.71) with the proton signal H-18 (δ_H 1.66), and the proton signal H-3 (δ_H 4.40) with the proton signals H-18 (δ_H 1.66) and of H-5 (δ_H 2.72) to suggest that H-1 was β-oriented, and H-2 and H-3 were α-oriented (Figure 3b). Because of the presence of chlorine as a heavy atom, the single crystal X-ray crystallographic analysis established the absolute configuration as follows: the hydroxyl groups at C-2 and C-3 were both of β-orientation, the chlorine at C-1 was of α-orientation

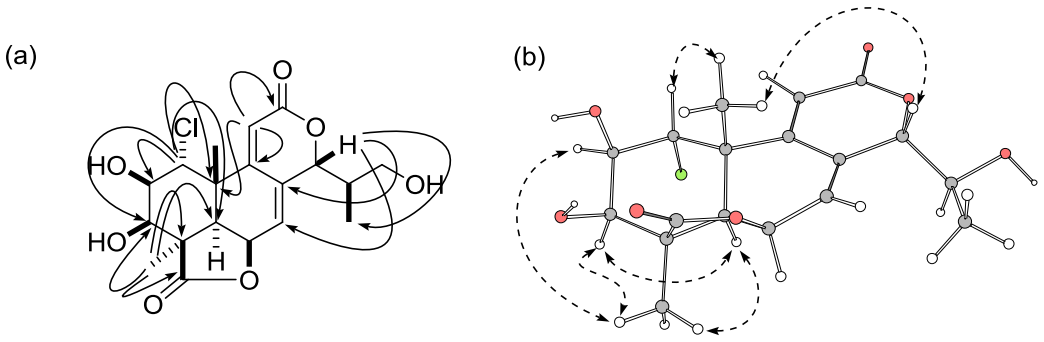

Figure 3. Selected HMBC (a) and NOESY (b) correlations of makilactone B (**2**).

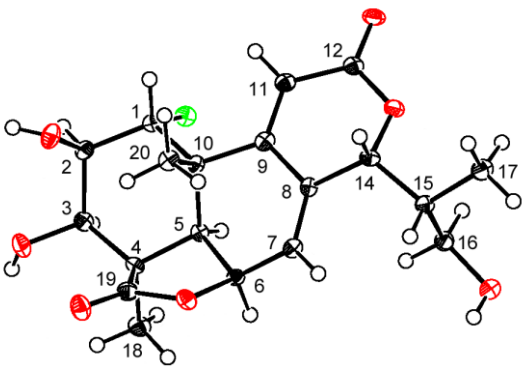

Figure 4. ORTEP representation of **2** as determined by single crystal X-ray crystallographic analysis.

and the configuration at C-15 was *R*, as shown in Figure 4. Accordingly, the structure of **2** was determined to be as shown in Figure 1.

Makilactone C (**3**) was isolated as colorless needles, mp 233℃. The molecular formula was determined to be $C_{19}H_{22}O_6$ from the [M^++Na] ion peak at *m/z* 369.1294 in HRESIMS. IR absorptions bands for γ-lactone carbonyl, δ-lactone carbonyl and hydroxyl groups were seen at 1770 cm^{-1}, 1702 cm^{-1} and 3430 cm^{-1}, respectively. The ^{13}C and ^1H NMR spectra of **3** were generally similar to those of **2**, implying that **3** had the nagilactone F unit with one double bond and one hydroxyl group. One methyl carbon signal at δ_c 15.4 was correlated with the doublet methyl proton signal at δ_H 1.42 to assign this methyl group to C-16 of the side chain. In the COSY spectrum, the methylene proton signals H-17 (δ_H 3.95 and δ_H 4.20) was correlated with the hydroxyl proton at δ_H 6.28, which implied the presence of a hydroxyl methyl group at C-15. These facts revealed that the side chain in **3** was the same in the structure as that in **2**. In the COSY spectrum, the proton signal of H-1 (δ_H 4.66) was correlated with the hydroxyl proton (δ_H 7.21) to show that the hydroxyl was at C-1. In ^{13}C NMR, the carbon signals of C-2 (δ_C 135.2) and of C-3 (δ_C 127.6) were in the lower magnetic field, implying the presence of a double bond between C-2 and C-3. The OH-1 proton signal (δ_H 7.21) was correlated with H-20 (δ_H 1.45) in the NOESY spectrum, suggesting that OH-1 was β-oriented. The single crystal X-ray crystallographic analysis demonstrated that the hydroxyl group at C-1 was β oriented and that the configuration at C-15 was *R** as shown in Figure 5. Accordingly, the structure of **3** was determined to be as shown in Figure 1.

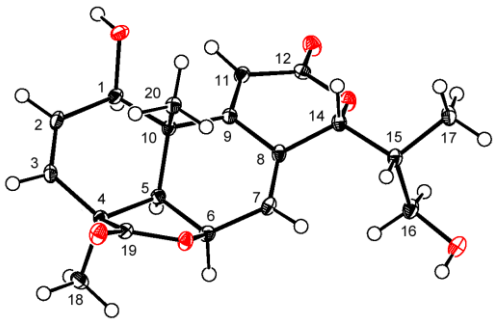

Figure 5. ORTEP representation of **3** as determined by single crystal X-ray crystallographic analysis.

Makilactone D (**4**) was isolated as colorless needles, mp 236 ℃. The molecular formula was determined to be $C_{19}H_{24}O_6$ from the [M^++Na] ion peak at *m/z* 371.1444 in HRESIMS. IR absorption bands for γ-lactone carbonyl, δ-lactone carbonyl and hydroxyl groups were observed at 1742 cm^{-1}, 1697 cm^{-1} and 3413 cm^{-1}, respectively. The ^{13}C and ^1H NMR spectra of **4** showing the presence of three methyl and two hydroxyl groups were generally quite similar to those of **3,** implying that **4** had the nagilactone F unit. One of the three methyl carbon signals, the one at δ_c 15.3 was correlated with the doublet methyl proton signal at δ_H 1.40, so that this methyl group was

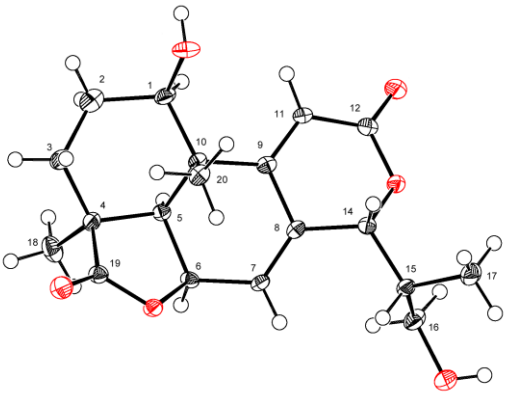

Figure 6. ORTEP representation of **4** as determined by single crystal X-ray crystallographic analysis.

assigned to C-16 in the side chain. The methylene proton signals of H-17 (δ_H 3.94 and δ_H 4.18) were correlated with the hydroxyl proton (δ_H 6.29) in the COSY spectrum, implying the presence of a hydroxyl methyl group connected to C-15. These facts revealed that the side chain in **4** was the same in the structure as that in **2** and **3**. In the COSY spectrum, the proton signal of H-1 (δ_H 4.10) was correlated with the hydroxyl proton at δ_H 6.70 to show the presence of OH at C-1. The hydroxy proton signal of OH-1 (δ_H 6.70) was correlated with the methyl proton signal of H-20 at δ_H 1.45 and the proton signal of H-1 at δ_H 4.10 was correlated with the proton signal of H-5 (δ_H 1.78) in the NOESY spectrum to suggest that H-1 was α-oriented. The single crystal X-ray crystallographic analysis confirmed that hydroxyl group at C-1 was of β-orientation and that the configuration at C-15 was *R** as shown in Figure 6. Accordingly, the structure of **4** was determined as shown in Figure 1.

The absolute configuration of chlorine-containing makilactone B (**2**) was established by X-ray crystallographic analysis. Since the CD spectra of all four compounds (**1**-**4**) showed negative Cotton effect, the absolute configurations of **1**-**4** were concluded to be the same, as shown Figure 1.

All these diterpenes isolated in the present study were tested for their cytotoxic activities on P388 murine leukemia cells and the results are given in Table **3**. The IC_{50} values of makilactone A (**1**) (0.050 μg/mL) and nagilactone F (0.090 μg/mL) were almost the same as that of the positive control used, camptothecin (0.045 μg/mL). Makilactones C (**3**) and D (**4**), 2α-hydroxynagolactone F[11] and 3β-hydroxynagilactone F[12] were slightly less active. The chlorinated dilactone, makilactone B (**2**) was almost inactive.

Table 3. IC_{50} values of makilactones A-D (**1**-**4**) against P388 murine leukemia cells.

compounds	IC_{50} (μg/mL)
makilactone A (**1**)	0.050
makilactone B (**2**)	80
makilactone C (**3**)	2.6
makilactone D (**4**)	0.75
nagilactone F	0.090
2α-hydroxy nagilactone F	0.20
3β-hydroxy nagilactone F	0.45
camptothecin	0.045

These norditerpenoid compounds which are characterized by having a γ-lactone unit between C-4 and C-6 and a δ-lactone unit between C-12 and C-14, are classified into three subgroups according to their B/C ring structure:[9] Subgroup A: having α-pyrone unit, Subgroup B: having 7α:8α-epoxy-9:11-enolide unit and Subgroup C: having 7:8, 9:11-dienolide unit. So far, not many norditerpenoids of Subgroup C have been reported. The presence of 7:8, 9:11-dienolide moiety as seen in Subgroup C is reported to be necessary for norditerpenoids to show a potent cytotoxic activity.[10] The compounds isolated in the present study all belong to Subgroup C and and all were shown to be active in the cytotoxicity assay (Table 3.). The present results may support the proposed relationship between the activity and the 7:8, 9:11-dienolide structure unit.

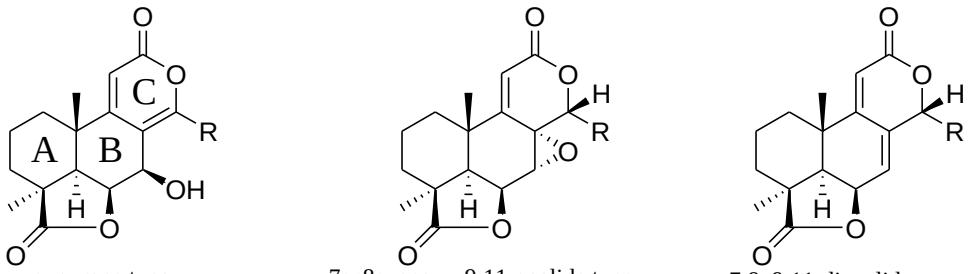

Figure 7. Calssification of bisnor- and norditerpene dilactones by Ito *et al*.[9]

EXPERIMENTAL

General Experimental Procedures

Optical rotations were measured on a JASCO DIP-360 automatic digital polarimeter, IR spectra on a JASCO FT/IR 620 spectrophotometer, and mass spectra on VG AutoSpec E and Micromass LCT (Manchester, UK) spectrometers. NMR spectra were obtained on a Brucker DRX-500 and on an AV-600 spectrometer at 300K in C_5D_5N. The chemical shifts (δ) of proton signals are given in ppm relative to the resonances of residual C_5D_4HN at 7.19 ppm and those of carbon signals in ppm relative to the resonance at 135.5 ppm for C_5D_5N. Silica gel (Merck Kiesel gel 60, 70-230 nm, Kanto silica gel N 60, 63-210 μm) and Diaion® HP-20 (Mitsubishi Chemical Co. Ltd.) were used for column chromatography and precoated Kieselgel 60 F_{254} (0.25 mm thick, Merck Co. Ltd.), RP–18 $F_{254}S$ (0.25 mm thick, Merck) plates for TLC, in which the spots were visualized by spraying of 10% H_2SO_4 solution, and subsequent heating. Preparative HPLC was carried out on a JASCO PU-986 equipped with a UV-970 UV detector (λ 220nm) and Inertsil PREP-ODS column (10 μm, 20 x 250 mm), by using MeOH/H_2O or MeCN/H_2O at a flow rate of 10mL/min. X-ray single crystallographic analysis was taken on a Mac Science DIP diffractometer with Mo Kα radiation (λ = 0.71073 Å).

Plant Material

Bark and root of *Podocarpus macrophyllus* D. Don collected in Kochi, Japan, in Nobember 2004 were air-dried. The botanical identification was made by K. Takeya, Professor of Plant Chemistry of Tokyo University of Pharmacy and Life Science. A voucher specimen (08JCP18) has been deposited in the herbarium of Tokyo University of Pharmacy and Life Science.

Extraction and isolation

The air dried bark of *Podocarpus macrophyllus* D. Don (3.2 kg) was extracted with hot MeOH (3 x 45 L). The combined MeOH extract was concentrated and the residue (284 g) was subjected to Diaion HP-20 resin column chromatography (10 cm x 40 cm) eluting sequentially with H_2O/MeOH (1:1, 2:8), MeOH,

and acetone (each 5 L) to give four fractions. The second fraction Fb (H_2O/MeOH 2:8) was concentrated to give a residue (10.4 g), which was subjected to silica gel column chromatography eluting with $CHCl_3$/MeOH (19:1) to give fractions Fb1-Fb12. Fb12 (145 mg) was subjected to ODS-HPLC eluting with H_2O/MeOH (54:46) to give **1** (3.1 mg), nagilactone F (2.5 mg) and 3β-hydroxylnagilactone F (3.0 mg).

The air dried root of *Podocarpus macrophyllus* D. Don (22.66 kg) was extracted with MeOH (45 L x 3) at room temperature. As described above for the bark, the MeOH extract was concentrated and the residue (614 g) was subjected to Diaion HP-20 resin column chromatography (10 cm x 40 cm) eluting with H_2O, H_2O/MeOH (1:1, 2:8), MeOH and acetone (each 5 L). Fractions Er (H_2O/MeOH 1:1) and Fr (H_2O/MeOH 2:8) were treated as follows. Fraction Er was concentrated to give a residue (71.6 g), which was subjected to silica gel chromatography eluting with $CHCl_3/H_2O$ (19:1) to give six fractions, Er1~Er6. Er2 (8.85 g) was further subjected to ODS-HPLC eluting with H_2O/MeCN (93.5:6.5) to give eleven fractions. The 10^{th} fraction gave **3** (6.1 mg).

Fraction Fr was concentrated to give a residue (82.4 g), which was subjected to silica gel column chromatography eluting sequentially with $CHCl_3/H_2O$ (1:0, 19:1, 9:1, 2:1, 0:1) to give five fractions Fr1~Fr5. Fraction Fr2 (12.6 g) was subjected to silica gel chromatography eluting with $CHCl_3/H_2O$ (30:1) to give fourteen fractions Fr2-1~Fr2-14. ODS-HPLC of Fr2-3 with H_2O/MeOH (60:40) gave 2α-hydroxynagilactone F (4.2 mg), that of Fr2-7 with H_2O/MeOH (77:23) gave **4** (5.7 mg), and that of Fr2-8 with H_2O/MeOH (75:25) gave **2** (19.6 mg).

Single crystal X-ray Crystallographic Analysis

For X-ray analysis, samples were recrystallized from EtOAc-MeCN-MeOH. Crystallographic data for **1**-**4** reported in this paper (Figure **2**-**5**) have been deposited at the Cambridge Crystallographic Data Centre, under the reference numbers CCDC 696338, 711930, 711929, and 711931, respectively. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.UK)

Assay of Cytotoxic Activity

The cytotoxic assay was performed by using the MTT assay method. The murine P388 leukemia cells were cultured in RPMI 1640 medium (Nissui Co. Ltd.) supplemented with 5% heat-inactivated fetal bovine serum (FBS) and kanamycin (5.3 mL/L) in a humidified atmosphere of 95% air and 5% CO_2 at 37 ℃. The 100 μL of the cell suspension was added to each well (3 x 10^3 cells/well) of a 96 microwell plate (Iwaki, flat bottomed, treated polystyrene) and the plate was incubated for 24 h. Test compounds were dissolved in DMSO in various concentrations (100, 30, 10, 3, 1, 0.3, 0.1 μg/mL) and 10 μl of the

test solution or DMSO (control) was added to each well. The plate was kept in an incubator at 37 ℃ for 48 h. After termination of the cell culture by adding 20 μL MTT (5% in PBS) to each well, the plate was further incubated for 4 h. To each well was added 100 μL of 10 % SDS in 0.01 N HCl. The plate was read on a microplate reader (MPR A4i, Tosoh) at 550 nm. A dose-response curve was plotted for each compound, and the concentrations giving 50 % inhibition of the cell growth (IC_{50}) were recorded.

Makilactone A (1) : Colorless needles, mp 236-239℃ (MeOH). $[\alpha]_D^{24}$-81.4° (*c* 0.16, MeOH); CD (*c* 0.000173, MeOH) λ (Δε) 265 (-13.6) nm. IR (film) 1702, 1769 (C=O) cm^{-1}, HRESIMS *m*/*z*:301.1444 [Calcd for $C_{18}H_{21}O_4$ 301.1440 (M^++H)]. ^{1}H- and ^{13}C- NMR, see Tables 1 and 2.

Makilactone B (2) : Colorless needles, mp 218℃ (MeOH). $[\alpha]_D^{24}$+101.5° (*c* 0.19, MeOH); CD (*c* 0.000113, MeOH) λ (Δε) 285 (-1.90) nm. IR (film) 1774, 1693 (C=O) cm^{-1}, 3311 (OH) cm^{-1}, HRESIMS *m*/*z*:421.1017 [Calcd for $C_{19}H_{23}O_7ClNa$ 421.1030 (M^++Na)]. ^{1}H- and ^{13}C NMR, see Tables 1 and 2.

Makilactone C (3) : Colorless needles, mp 233℃ (MeOH). $[\alpha]_D^{24}$-219.9 (*c* 0.06, MeOH); CD (*c* 0.000172, MeOH) λ (Δε) 268 (-12.6) nm. IR (film) 1770, 1702 (C=O) cm^{-1}, 3430 (OH) cm^{-1}, HRESIMS *m*/*z*: 369.1294 [Calcd for $C_{19}H_{22}O_6Na$ 369.1314 (M^++Na)]. ^{1}H- and ^{13}C NMR, see Tables 1 and 2.

Makilactone D (4) : Colorless needles, mp 236℃ (MeOH). $[\alpha]_D^{24}$-185.3 (*c* 0.08, MeOH); CD (*c* 0.000147, MeOH) λ (Δε) 267 (-11.0) nm. IR (film) 1742, 1697 (C=O) cm^{-1}, 3413 (OH) cm^{-1}, HRESIMS *m*/*z*: 371.1444 [Calcd for $C_{19}H_{24}O_6Na$ 371.1471 (M^++Na)]. ^{1}H- and ^{13}C NMR, see Tables 1 and 2.

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