Triterpenoids from the Fruits of *Phellodendron chinense* SCHNEID.: The Stereostructure of Niloticin

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Three tirucallane-type triterpenoids, niloticin, phellochin and melianone, were isolated from the fruits of *Phellodendron chinense* SCHNEID. (Rutaceae). The stereostructure of niloticin was determined based on spectroscopic and X-ray crystal structure analyses. Furthermore, a derivative of niloticin and two derivatives of melianone were also found. A possible biogenetic pathway in *P. chinense* is proposed: niloticin → melianone → limonoids, on the basis of isolation of the compounds in different oxidation states.

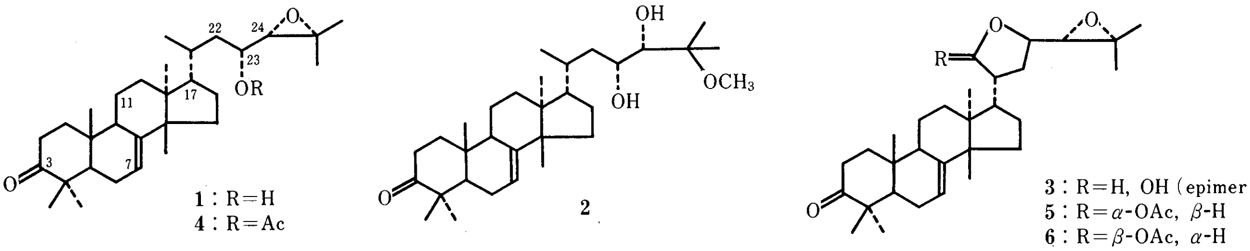
Keywords stereostructure; X-ray analysis; niloticin; phellochin; melianone; *Phellodendron chinense*; triterpenoid; limonoid

The barks of *Phellodendron* species (Rutaceae) have been used traditionally as antidiarrheic, antiphlogistic, disinfectant, and stomachic agents,[1,2] and also as an ophthalmic medicine.[3] A number of papers have been published on the active principles of genus *Phellodendron*, but little work has been done on *Phellodendron chinense* SCHNEID.,[4,5] particularly on its fruit.[6-8] We have isolated limonoids and alkaloids from the bark of *P. amurense* RUPR. as potent antifeedants against termites (*Reticulitermes speratus*).[9,10] Further research on the fruits of *P. chinense* resulted in the isolation of tirucallane-type triterpenoids, niloticin (**1**),[11] melianone (**3**)[12,13] and phellochin (**2**). An X-ray study has enabled us to elucidate the configuration of niloticin.

Melianone (**3**) isolated above was investigated by comparison of its spectral data ^{13}C-nuclear magnetic resonance (^{13}C-NMR), ^{1}H-NMR and two dimensional-NMR (2D-NMR) with those of an authentic sample[12-14] and it was concluded to be a mixture of epimers at C-21 from the result of acetylation, which yielded 21-α-acetoxy- (**5**) and 21-β-acetoxy- (**6**) melianones.

Niloticin (**1**) was obtained as colorless needles, mp 149—151 °C, $[\alpha]_D^{25}$ $-82.6°$ ($c=1.0$, MeOH). Its ^{1}H-NMR and ^{13}C-NMR spectral data were similar to literature data[8] [lit. mp 147 °C $[\alpha]_D$ $-62°$ ($c=0.08$, CHCl$_3$)].

Although niloticin has been isolated from *Turraea nilotica*[11] and *P. chinense*,[8] its stereochemistry has not been determined. To confirm its stereochemistry unequivocally, **1** was studied by X-ray diffraction analysis. Crystals of **1** obtained by slow crystallization from hexane–acetone were



1 : R=H
4 : R=Ac

2

3 : R=H, OH (epimer)
5 : R=α-OAc, β-H
6 : R=β-OAc, α-H

Chart 1

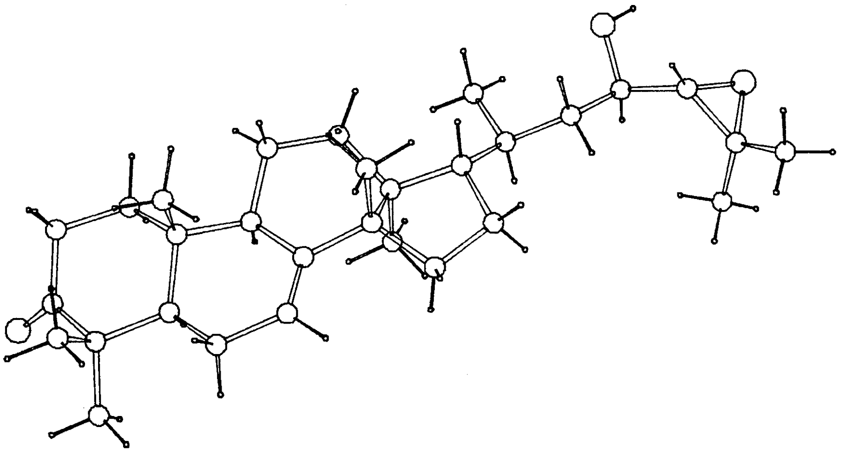


Fig. 1. Perspective View of Niloticin (**1**)

Table I. Atomic Coordinates and Equivalent Isotropic Thermal Parameters for Non-hydrogen Atoms

Atom	x	y	z	B_{eq} (Å^2)
O(1)	0.4707 (1)	0.0 (0)	0.8652 (2)	8.04 (21)
O(2)	0.2460 (1)	0.5530 (6)	0.1333 (2)	5.91 (18)
O(3)	0.2971 (1)	0.8231 (6)	0.0048 (1)	5.49 (16)
C(1)	0.3690 (2)	0.1540 (7)	0.7264 (2)	4.67 (18)
C(2)	0.3824 (2)	0.1035 (8)	0.8159 (2)	5.43 (23)
C(3)	0.4428 (2)	0.1333 (3)	0.8373 (2)	5.33 (22)
C(4)	0.4659 (1)	0.3360 (8)	0.8209 (2)	4.80 (22)
C(5)	0.4465 (1)	0.4015 (6)	0.7333 (2)	4.01 (17)
C(6)	0.4645 (1)	0.6107 (7)	0.7143 (2)	4.27 (18)
C(7)	0.4427 (1)	0.6786 (6)	0.6326 (2)	3.82 (16)
C(8)	0.4045 (1)	0.5879 (6)	0.5862 (2)	3.44 (16)
C(9)	0.3814 (1)	0.3914 (6)	0.6120 (2)	3.70 (16)
C(10)	0.3846 (1)	0.3668 (6)	0.7056 (2)	3.78 (17)
C(11)	0.3240 (1)	0.3492 (7)	0.5707 (2)	4.47 (21)
C(12)	0.3206 (1)	0.3713 (7)	0.4782 (2)	4.68 (18)
C(13)	0.3638 (1)	0.5126 (6)	0.4448 (2)	3.60 (16)
C(14)	0.3788 (1)	0.6740 (6)	0.5088 (2)	3.53 (16)
C(15)	0.4141 (1)	0.8146 (6)	0.4609 (2)	4.22 (19)
C(16)	0.3854 (1)	0.8122 (6)	0.3750 (2)	4.25 (20)
C(17)	0.3442 (1)	0.6386 (6)	0.3712 (2)	3.82 (16)
C(18)	0.4165 (1)	0.3966 (6)	0.4260 (2)	4.22 (16)
C(19)	0.3452 (1)	0.5117 (8)	0.7433 (2)	4.86 (23)
C(20)	0.3357 (1)	0.5469 (6)	0.2863 (2)	4.10 (17)
C(21)	0.3004 (2)	0.3629 (7)	0.2832 (2)	5.77 (22)
C(22)	0.3116 (2)	0.7047 (7)	0.2281 (2)	4.36 (18)
C(23)	0.2986 (1)	0.6522 (7)	0.1400 (2)	4.52 (21)
C(24)	0.2949 (1)	0.8372 (7)	0.0917 (2)	4.53 (18)
C(25)	0.3415 (1)	0.9286 (7)	0.0517 (2)	4.71 (19)
C(26)	0.3413 (2)	1.1454 (8)	0.0419 (2)	5.86 (23)
C(27)	0.3971 (2)	0.8290 (10)	0.0506 (3)	6.57 (25)
C(28)	0.4474 (2)	0.4733 (8)	0.8888 (2)	6.11 (23)
C(29)	0.5295 (2)	0.3280 (10)	0.8285 (3)	6.97 (26)
C(30)	0.3265 (2)	0.7899 (7)	0.5316 (2)	4.88 (22)

Table II. Atomic Coordinates for Hydrogen Atoms

Atom	x	y	z
H02	0.237 (2)	0.513 (9)	0.076 (2)
H1A	0.388 (2)	0.066 (8)	0.692 (2)
H1B	0.327 (2)	0.141 (8)	0.713 (2)
H2A	0.359 (2)	0.190 (8)	0.853 (2)
H2B	0.371 (2)	−0.037 (9)	0.826 (2)
H5	0.466 (2)	0.306 (8)	0.700 (2)
H6A	0.451 (2)	0.701 (8)	0.757 (3)
H6B	0.506 (2)	0.617 (8)	0.719 (3)
H7	0.459 (2)	0.803 (8)	0.611 (3)
H9	0.406 (2)	0.284 (8)	0.590 (2)
H11A	0.313 (2)	0.211 (8)	0.585 (2)
H11B	0.297 (2)	0.440 (8)	0.595 (2)
H12A	0.324 (2)	0.242 (8)	0.452 (2)
H12B	0.282 (2)	0.428 (8)	0.461 (2)
H15A	0.414 (2)	0.951 (8)	0.485 (2)
H15B	0.453 (2)	0.764 (8)	0.461 (2)
H16A	0.365 (2)	0.941 (8)	0.365 (2)
H16B	0.413 (2)	0.796 (8)	0.332 (2)
H17	0.305 (2)	0.678 (8)	0.380 (2)
H18A	0.444 (2)	0.489 (9)	0.405 (2)
H18B	0.407 (2)	0.298 (8)	0.385 (3)
H18C	0.432 (2)	0.337 (8)	0.477 (2)
H19A	0.356 (2)	0.648 (9)	0.729 (3)
H19B	0.347 (2)	0.493 (8)	0.802 (2)
H19C	0.306 (2)	0.485 (9)	0.720 (2)
H20	0.373 (2)	0.502 (9)	0.268 (2)
H21A	0.294 (2)	0.312 (9)	0.228 (2)
H21B	0.261 (2)	0.403 (8)	0.301 (2)
H21C	0.315 (2)	0.262 (8)	0.320 (3)
H22A	0.277 (2)	0.753 (8)	0.251 (3)
H22B	0.339 (2)	0.817 (9)	0.231 (2)
H23	0.330 (2)	0.564 (8)	0.119 (3)
H24	0.270 (2)	0.903 (8)	0.128 (3)
H26A	0.370 (2)	1.205 (9)	0.076 (3)
H26B	0.303 (2)	1.201 (9)	0.057 (2)
H26C	0.345 (2)	1.183 (9)	−0.015 (3)
H27A	0.425 (2)	0.902 (9)	0.087 (2)
H27B	0.409 (2)	0.819 (9)	−0.002 (3)
H27C	0.395 (2)	0.695 (9)	0.076 (3)
H28A	0.462 (2)	0.607 (8)	0.885 (3)
H28B	0.462 (2)	0.419 (8)	0.945 (2)
H28C	0.406 (2)	0.473 (9)	0.889 (2)
H29A	0.547 (2)	0.456 (9)	0.819 (2)
H29B	0.544 (2)	0.229 (8)	0.787 (2)
H29C	0.543 (2)	0.279 (8)	0.883 (3)
H30A	0.307 (2)	0.851 (9)	0.483 (3)
H30B	0.337 (2)	0.893 (9)	0.571 (2)
H30C	0.300 (2)	0.701 (9)	0.558 (2)

monoclinic with space group $C2$, $C_{30}H_{48}O_3$, M_r 456.7, $a=24.169$ (2), $b=6.811$ (1), $c=16.573$ (2) Å, $\beta=93.48°$ (1), $V=2723.1$ Å^3, $Z=4$, $D_{cal}=1.114$ g/cm^3. Intensity data of 1994 reflections within $2\theta<120°$ were collected by using a four circle diffractometer, with graphite-monochromated Cu $K\alpha$ radiation ($\lambda=1.54178$ Å), and 1924 unique reflections with $F_0<3\sigma$ (F) were used for the structure determination ($R_{int}=0.025$). The crystal structure was solved using the RANTAN program[15] and was refined by the block-diagonal least-squares method. The hydrogen atoms were located by difference Fourier synthesis and refined isotropically. The final R value was 0.0507 ($\omega R=0.0657$, S$=1.73$). Parameters of atoms, bond lengths and bond angles are listed in Tables I—IV. A perspective view of the molecular structure of **1** is shown in Fig. 1. It was clearly shown to be a tirucallane-type, but not a euphane-type triterpenoid.

Phellochin (**2**) was obtained as colorless needles, mp 173—175 °C $[\alpha]_D^{25}$ −84.8° ($c=0.10$, MeOH) and the molecular formula was $C_{31}H_{52}O_4$ ($M^+=488.3747$ by high resolution mass spectrum (HRMS), formula requires 488.3866). The base peak at m/z 73 ($C_4H_9O^+$) in the electron impact-mass spectrum (EI-MS) revealed that the methoxyl is bonded to C-25 bearing two tertiary methyls. The fragments of m/z 369 and m/z 370 suggested that **2** would have the same skelton as **1**. Its NMR spectral data (both ^{13}C and ^{1}H) were very similar to those of niloticin except for the side chain (Table V). From the ^{1}H-NMR spectrum, the sharp signals at 3.52 ppm (d, $J=1.65$ Hz, 1H) and 2.65 ppm (d, $J=9.89$ Hz, 1H) coupled with the C-23 and C-24 protons, respectively, but they were not observed to couple with any carbon in the ^{1}H–^{13}C 2D-NMR spectrum. After deuteration, both signals had disappeared. On the other hand, the signals at 4.09 ppm (ddd, $J=8.94$, 4.94, 1.65 Hz, H-23) and 3.13 ppm (d, $J=9.89$ Hz, H-24) were simplified to a doublet of doublets ($J=8.94$, 4.94 Hz) and a singlet, respectively, by the deuteration. Biogenetic considerations and the optical rotations suggested that the configuration of **2** might be the same as that of **1**. The coupling constant of H-23 and H-24 could not be observed at in the ^{1}H-NMR spectrum (400 MHz) whereas these two vicinal protons were observed to couple with 23-C–O$\underline{\mathrm{H}}$ (1.65 Hz) and 24-C–O$\underline{\mathrm{H}}$ (9.89 Hz), respectively. The presence of the two sharp doublet signals owing to hydroxy

Table III. Bond Lengths (Å) for Niloticin with Estimated Standard Deviations in Parentheses

Atom	Bond length (e.s.d.)	Atom	Bond length (e.s.d.)
O(1)–C(3)	1.206 (5)	O(2)–C(23)	1.438 (4)
O(3)–C(24)	1.448 (4)	O(3)–C(25)	1.473 (4)
C(1)–C(2)	1.538 (5)	C(1)–C(10)	1.542 (6)
C(2)–C(3)	1.495 (7)	C(3)–C(4)	1.520 (7)
C(4)–C(5)	1.563 (5)	C(4)–C(28)	1.550 (6)
C(4)–C(29)	1.536 (5)	C(5)–C(6)	1.528 (6)
C(5)–C(10)	1.556 (4)	C(6)–C(7)	1.496 (5)
C(7)–C(8)	1.319 (4)	C(8)–C(9)	1.521 (5)
C(8)–C(14)	1.509 (5)	C(9)–C(10)	1.558 (5)
C(9)–C(11)	1.536 (4)	C(10)–C(19)	1.531 (5)
C(11)–C(12)	1.538 (5)	C(12)–C(13)	1.547 (5)
C(13)–C(14)	1.555 (5)	C(13)–C(17)	1.542 (5)
C(13)–C(18)	1.547 (4)	C(14)–C(15)	1.535 (5)
C(14)–C(30)	1.556 (6)	C(15)–C(16)	1.545 (4)
C(16)–C(17)	1.545 (5)	C(17)–C(20)	1.542 (5)
C(20)–C(21)	1.515 (6)	C(20)–C(22)	1.535 (6)
C(22)–C(23)	1.517 (5)	C(23)–C(24)	1.493 (6)
C(24)–C(25)	1.479 (5)	C(25)–C(26)	1.486 (7)
C(25)–C(27)	1.506 (6)		

Table IV. Bond Angles (°) for Niloticin with Estimated Standard Deviations in Parentheses

Atom	Angle (e.s.d.)	Atom	Angle (e.s.d.)
C(24)–O(3)–C(25)	60.8 (2)	C(2)–C(1)–C(10)	112.7 (3)
C(1)–C(2)–C(3)	110.1 (4)	O(1)–C(3)–C(2)	120.3 (5)
O(1)–C(3)–C(4)	123.3 (4)	C(2)–C(3)–C(4)	116.4 (4)
C(3)–C(4)–C(5)	109.4 (3)	C(3)–C(4)–C(28)	107.0 (3)
C(3)–C(4)–C(29)	109.3 (4)	C(5)–C(4)–C(28)	114.7 (4)
C(5)–C(4)–C(29)	109.2 (3)	C(28)–C(4)–C(29)	107.1 (4)
C(4)–C(5)–C(6)	112.6 (3)	C(4)–C(5)–C(10)	117.3 (3)
C(6)–C(5)–C(10)	111.2 (3)	C(5)–C(6)–C(7)	112.7 (3)
C(6)–C(7)–C(8)	125.3 (4)	C(7)–C(8)–C(9)	120.3 (3)
C(7)–C(8)–C(14)	123.4 (4)	C(9)–C(8)–C(14)	116.2 (3)
C(8)–C(9)–C(10)	112.2 (3)	C(8)–C(9)–C(11)	112.1 (3)
C(10)–C(9)–C(11)	114.4 (2)	C(1)–C(10)–C(5)	108.7 (3)
C(1)–C(10)–C(9)	109.0 (3)	C(1)–C(10)–C(19)	110.4 (3)
C(5)–C(10)–C(9)	105.4 (2)	C(5)–C(10)–C(19)	113.1 (3)
C(9)–C(10)–C(19)	110.0 (3)	C(9)–C(11)–C(12)	114.7 (2)
C(11)–C(12)–C(13)	114.9 (3)	C(12)–C(13)–C(14)	109.3 (3)
C(12)–C(13)–C(17)	116.6 (2)	C(12)–C(13)–C(18)	109.7 (3)
C(14)–C(13)–C(17)	101.2 (3)	C(14)–C(13)–C(18)	109.7 (2)
C(17)–C(13)–C(18)	110.0 (3)	C(8)–C(14)–C(13)	111.8 (3)
C(8)–C(14)–C(15)	118.0 (2)	C(8)–C(14)–C(30)	106.8 (3)
C(13)–C(14)–C(15)	101.7 (3)	C(13)–C(14)–C(30)	111.4 (2)
C(15)–C(14)–C(30)	107.1 (3)	C(14)–C(15)–C(16)	103.7 (2)
C(15)–C(16)–C(17)	107.3 (3)	C(13)–C(17)–C(16)	103.1 (2)
C(13)–C(17)–C(20)	120.9 (3)	C(16)–C(17)–C(20)	113.4 (3)
C(17)–C(20)–C(21)	114.2 (3)	C(17)–C(20)–C(22)	108.3 (3)
C(21)–C(20)–C(22)	111.5 (3)	C(20)–C(22)–C(23)	119.2 (4)
O(2)–C(23)–C(22)	108.4 (3)	O(2)–C(23)–C(24)	109.3 (3)
C(22)–C(23)–C(24)	108.6 (4)	O(3)–C(24)–C(23)	118.2 (4)
O(3)–C(24)–C(25)	60.5 (2)	C(23)–C(24)–C(25)	125.0 (3)
O(3)–C(25)–C(24)	58.7 (2)	O(3)–C(25)–C(26)	115.4 (3)
O(3)–C(25)–C(27)	113.3 (4)	C(24)–C(25)–C(26)	118.0 (3)
C(24)–C(25)–C(27)	121.3 (4)	C(26)–C(25)–C(27)	116.3 (4)

protons suggests that the side chain may form two intramolecular hydrogen bonds. The hydrogen bonds fix the dihedral angle of the vicinal protons (H-23 and H-24) at around 90 degrees.

Comparing the structure of **2** with that of **1**, it appears that the former might be an artifact derived from the latter by methanolysis of the epoxy ring,[11] because the fruits of *P. chinense* had been steeped in MeOH for a long period.

Table V. The ^{13}C-NMR Chemical Shifts for the Side Chains of Compounds **1**, **2**, **4**, **5** and **6**

	C-20	C-21	C-22	C-23	C-24	C-25
1	33.57	19.91	40.72	69.27	68.47	60.28
2	33.73	18.93	39.86	68.72	76.39	79.81
4	33.29	19.91	38.51	72.09	65.39	59.32
5	47.39	100.71	33.83	78.95	64.97	57.03
6	45.38	96.91	30.83	79.84	66.88	57.14

All spectra were measured in $CDCl_3$, at 100 MHz.

Limonolids are common in Rutaceae and Meliaceae. One of the characteristic features in the common structure of limonoids is the existence of a furan ring. Melianone is an important intermediate in the furan ring formation because of its oxidized and ring-forming carbon at C-21. The proposed biogenetic pathway from melianone to limonoids is supported by the results of organic reactions[16] and also was confirmed by the isolation of compounds in various oxidation states from a same plant.[12,17] Our studies on barks of *Phellodendron* spp. resulted in the isolation of limonoids.[10] Compounds **1**, **2** and melianone have different oxidation states at the side chain and have the same stereochemical properties. These considerations suggest that the possible biogenetic pathway in *P. chinense* may be as follows: niloticin (in the fruits)→melianone (in the fruits)→limonoids (in the bark).

Experimental

All the melting points were determined on a Yanagimoto micro-apparatus without any correction. Infrared (IR) spectra were run with a Shimadzu IR-460 instrument (KBr). ^{1}H-NMR spectra were recorded with a JEOL GSX-400 (400 MHz) spectrometer and ^{13}C-NMR spectra with JEOL GSX-400 (100 MHz) spectrometer in $CDCl_3$ as the solvent and tetramethylsilane (TMS) as internal standard. MS were measured with a JMS-DX 303 (JEOL) using a direct inlet system. For column chromatography and thin-layer chromatography (TLC), BW-300 (Fuji Davison) silica gel and pre-coated silica gel plates (Macherey-Nagel, G/UV$_{254}$) were used, respectively, and for analyses and separations high performance liquid chromatography (HPLC, Hitachi, 655A-11) with a silica gel column and/or a 5-C_{18} ODS column was used. The X-ray analysis of **1** was performed in Kyoto University. Intensity data were collected with a Rigaku AFC-5RU diffractometer using Cu $K\alpha$ radiation. The structure analysis was undertaken on a FACOM H780 in the Data Processing Center of Kyoto University using the program system KPPXRAY.[18]

Plant Material Fruits of *P. chinense* were collected in 1987 at the garden of medicinal plants of Kyoto Pharmaceutical University and dried under room conditions.

Isolation of 1—3 The dried fruits (618 g) were crushed and extracted twice with MeOH (total 10 l) at room temperature over 10 d. The extracts (264 g) were suspended in H_2O and partitioned with hexane. The hexane layer (30.1 g) was chromatographed on silica gel by hexane–acetone (10 : 1), and niloticin (3.30 g), phellochin (100 mg) and melianone (0.80 g) were isolated.

Niloticin (1) Colorless needles, mp 149—151 °C, $[\alpha]_D^{25}$ $-82.6°$ ($c=1.0$, MeOH). IR ν_{max}^{KBr} (cm^{-1}): 3470, 1700. ^{1}H-NMR δ (ppm): 5.32 (dd, $J=2.20$, 5.50 Hz, H-7), 3.56 (m, H-23), 2.76 (dt, $J=5.50$, 14.26 Hz, H-2), 2.66 (d, $J=8.24$ Hz, H-24), 2.26 (m, H-2), 1.33, 1.32. 1.12, 1.05, 1.03, 1.01, 0.82 (s, 21H), 0.96 (d, $J=6.05$ Hz, 3H) and 1.00—2.20 (m, 19H). ^{13}C-NMR (ppm): 216.90 (s), 145.75 (s), 118.03 (d), 69.27 (d), 68.47 (d), 60.28 (s), 53.30 (d), 52.37 (d), 51.26 (s), 48.52 (d), 47.90 (s), 43.60 (s), 40.72 (t), 38.58 (t), 35.06 (s), 34.94 (t), 34.04 (t), 33.64 (t), 33.57 (d), 28.78 (t), 27.41 (q), 24.89 (q), 24.57 (q), 24.39 (t), 21.79 (q), 21.62 (q), 19.91 (q), 19.84 (q), 18.29 (t), 12.82 (q). MS m/z (%): 456 (M^+, 17), 370 (29), 369 (100), 351 (30), 325 (62), 95 (47).

Phellochin (2) Colorless needles, mp 173—175 °C, $[\alpha]_D^{25}$ −84.8° (c=0.10, MeOH). IR ν_{max}^{KBr} (cm^{-1}): 3530, 3430, 1690. ^{1}H-NMR δ (ppm): 5.31 (dd, J=2.20, 5.49 Hz, H-7), 4.09 (ddd, J=1.65, 4.94, 8.94 Hz, H-23), 3.52 (d, J=1.65 Hz, 23-OH), 3.25 (s, OCH_3), 3.13 (d, J=9.89 Hz, H-24), 2.76 (dt, J=5.49, 14.26 Hz, H-2), 2.65 (d, J=9.89 Hz, 24-OH), 2.26 (m, H-2), 1.30, 1.23, 1.11, 1.05, 1.01, 1.00, 0.82 (s, 21H), 0.93 (d, J=6.60 Hz, 3H) and 1.10—2.20 (m, 16H). ^{13}C-NMR (ppm): 216.97 (s), 145.93 (s), 118.03 (d), 79.81 (s), 76.39 (d), 68.72 (d), 53.80 (d), 52.38 (d), 51.25 (s), 49.36 (q), 48.53 (d), 47.92 (s), 43.80 (s), 39.86 (t), 38.59 (t), 35.06 (s), 34.97 (t), 34.04 (t), 33.80 (t), 33.73 (d), 28.50 (t), 27.41 (q), 24.58 (q), 24.40 (t), 22.07 (q), 21.65 (q), 21.60 (q), 18.93 (q), 18.35 (t), 12.85 (q). MS m/z (%): 488 (M^+, 5), 398 (31), 384 (25), 370 (31), 369 (98), 351 (32), 325 (48), 73 (100).

Melianone (3) Colorless needles, mp 212—214 °C [lit. 209—211 °C]. Both ^{1}H-NMR and ^{13}C-NMR spectral data are similar to reported data.[12]

Acetylation of 1 A solution of **1** (20.0 mg) in a mixture of 5.0 ml of dry ether and 2.0 ml of dry pyridine was shaken with 2.0 ml of Ac_2O and kept for 24 h at room temperature, and compound **4** (16.0 mg) was obtained as colorless needles, mp 157—158.5 °C, $[\alpha]_D^{25}$ −68° (c=0.195, MeOH) [lit.[8] 157 °C, $[\alpha]_D$ −75° (c=0.035, $CHCl_3$)]. IR ν_{max}^{KBr} (cm^{-1}): 1733, 1702. ^{1}H-NMR δ (ppm): 5.32 (dd, J=2.20, 5.50 Hz, H-7), 4.87 (m, H-23), 2.74 (dt, J=5.49, 14.26 Hz, H-2), 2.73 (d, J=8.24 Hz, H-24), 2.27 (m, H-2), 2.07 (s, OAc, 3H), 1.37, 1.33, 1.12, 1.05, 1.01, 1.00, 0.81 (s, 21H), 0.97 (d, J=6.04 Hz, 3H) and 1.00—2.30 (m, 18H). ^{13}C-NMR (ppm): 216.84 (s), 170.33 (s), 145.65 (s), 118.09 (d), 72.09 (d), 65.39 (d), 59.32 (s), 53.03 (d), 52.34 (d), 51.26 (s), 48.47 (d), 47.89 (s), 43.58 (s), 38.55 (t), 38.51 (t), 35.05 (s), 34.93 (t), 33.99 (t), 33.59 (t), 33.29 (d), 28.73 (t), 27.38 (q), 24.70 (q), 24.57 (q), 24.38 (t), 21.75 (q), 21.62 (q), 21.30 (q), 19.91 (q), 19.59 (q), 18.25 (t), 12.80 (q). MS m/z (%): 498 (M^+, 90), 483 (100), 465 (33), 423 (82), 405 (32), 369 (58), 325 (63).

Acetylation of 3 Compound **3** (25.0 mg) was acetylated with 2.5 ml of Ac_2O under the same conditions as above, and a mixture of **5** and **6** was obtained. The mixture was separated by HPLC using a silica gel column with hexane–AcOEt (10 : 2) as the solvent. Pure **5** (12.6 mg) and **6** (9.0 mg) were obtained.

5 Colorless sticky oil, $[\alpha]_D^{25}$ −68° (c=0.122, MeOH). IR ν_{max}^{KBr} (cm^{-1}): 1740, 1701. ^{1}H-NMR δ (ppm): 6.18 (d, J=3.84 Hz, H-21), 5.31 (dd, J=2.20, 5.50 Hz, H-7), 3.88 (dt, J=7.14, 9.89 Hz, H-23), 2.72 (dt, J=5.50, 14.29 Hz, H-2), 2.66 (d, J=7.70 Hz, H-24), 2.06 (s, OAc, 3H), 1.33, 1.31, 1.12, 1.04, 1.03, 1.01, 0.83 (s, 21H), 1.00—2.40 (m, 19H). ^{13}C-NMR (ppm): 216.74 (s), 170.34 (s), 145.39 (s), 118.36 (d), 100.71 (d), 78.95 (d), 64.97 (d), 57.03 (s), 54.41 (d), 51.03 (d), 50.36 (s), 48.31 (d), 47.87 (s), 47.39 (d), 43.64 (s), 38.48 (t), 35.12 (d), 34.90 (t), 34.27 (t), 33.83 (t), 31.83 (t), 27.46 (t), 27.34 (q), 24.93 (q), 24.55 (q), 24.41 (t), 22.83 (q), 21.59 (q), 21.41 (q), 19.53 (q), 17.75 (t), 12.76 (q). MS m/z (%): 512 (M^+, 10), 497 (16), 453 (18), 452 (21), 438 (36), 437 (100), 381 (22), 366 (22), 365 (60), 297 (20), 271 (12).

6 Colorless needles, mp 178—180 °C, $[\alpha]_D^{25}$ +6° (c=0.075, MeOH). IR ν_{max}^{KBr} (cm^{-1}): 1740, 1702. ^{1}H-NMR δ (ppm): 6.21 (d, J=2.75 Hz, H-21), 5.33 (dd, J=2.20, 5.50 Hz, H-7), 3.89 (ddd, J=5.50, 7.14, 9.89 Hz, H-23), 2.74 (d, J=7.14 Hz, H-24), 2.73 (dt, J=5.49, 14.26 Hz, H-2), 2.06 (s, OAc, 3H), 1.33, 1.31, 1.12, 1.04, 1.03, 1.01, 0.83 (s, 21H) and 1.00—2.50 (m, 19H). ^{13}C-NMR (ppm): 216.74 (s), 170.01 (s), 145.33 (s), 118.46 (d), 96.91 (d), 79.84 (d), 66.88 (d), 57.14 (s), 52.37 (d), 50.90 (d), 48.17 (s), 47.86 (d), 46.01 (s), 45.38 (d), 43.54 (s), 38.40 (t), 35.15 (d), 34.90 (t), 34.18 (t), 31.70 (t), 27.57 (t), 27.22 (q), 24.97 (q), 24.58 (q), 24.42 (t), 22.91 (q), 21.60 (q), 21.60 (q), 19.38 (q), 17.63 (t), 12.74 (q). MS m/z (%): 512 (M^+, 52), 497 (15), 453 (24), 452 (40), 438 (35), 437 (100), 381 (25), 366 (29), 365 (88), 297 (23), 271 (20).

References

1) W. H. Lewis and P. F. Elvin-Lewis, "Medical Botany: Plants Affecting Man's Health," John Wiley and Sons, Inc., New York, 1977, p. 345.

2) K. Kimura and T. Kimura, "Medicinal Plants of Japan in Color," Hoikusha Publishing Co., Ltd., Osaka, 1977, pp. 49, 139.

3) T. Namba, "Colored Illustrations of Wakan-Yaku," Vol. II, Hoikusha Publishing Co., Ltd., Osaka, 1986, p. 148.

4) Y. Zhang, Faming Zhuanli Shenqing Shuomingshu CN 85108076 A, Sep. 1986.

5) L. Chen, W. Liang, and X. Xu, *Zhongcaoyao*, **12**, 36 (1981).

6) L. Li and J. Ye, *Yaoxue Tongbao*, **17**, 304 (1982).

7) D. A. Murav'eva, V. A. Chelombit'ko, and N. P. Kir'yalov, *Aktual. Probl. Izuch. Efirnomaslich. Rast. Efirn.*, Masel 139 (1970).

8) A. I. Gray, P. Bhandari, and G. Waterman, *Phytochemistry*, **27**, 1805 (1988).

9) M. Kim, H. Kawaguchi, M. Isida, T. Yamamoto, S. Takahashi, R. Yamaoka, M. Kozuka, and K. Goto, The 16th International Symposium on the Chemistry of Natural Products, 1988, p. 485.

10) H. Kawaguchi, M. Kim, M. Ishida, Y. J. Ahn, T. Yamamoto, R. Yamaoka, M. Kozuka, K. Goto, and S. Takahashi, *Agric. Biol. Chem.*, **53**, 2635 (1989).

11) D. A. Mulholland and D. A. H. Taylor, *Phytochemistry*, **27**, 1220 (1988).

12) T. Nakanishi, A. Inada, and D. Lavie, *Chem. Pharm. Bull.*, **34**, 100 (1986).

13) T. Nakanishi, A. Inada, M. Nishi, T. Miki, R. Hino, and T. Fujiwara, *Chem. Lett.*, **1986**, 69.

14) A. B. Kunda, S. Ray, and A. Chatterjee, *Phytochemistry*, **24**, 2123 (1985).

15) Y. Jia-Xing, *Acta Cryst., Sect. A*, **37**, 642 (1981).

16) K. Nakanishi, T. Goto, S. Ito, S. Natori, and S. Nozoe, "Natural Products Chemistry," Vol. 1, Kodansha Academic Press, Tokyo, 1974, p. 392.

17) I. Kubo, A. Matsumoto, and T. Matsumoto, *Tetrahedron*, **42**, 489 (1986).

18) T. Taga, T. Higashi, and H. Iizuka, KPPXRAY, Kyoto Program Package for X-Ray Analysis, Univ. of Kyoto, 1980.