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NEW ANISATIN-LIKE SESQUITERPENE LACTONES FROM PERICARPS OF ILLICIUM MAJUS

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Abstract: Two new sesquiterpene lactones, isolated from the pericarps of Illicium majus together with anisatin, have been assigned structures with an anisatin skeleton on the basis of detailed spectroscopic analysis and established by an X-ray diffraction method.

Illicium majus(Illiciaceae) is a Chinese Illicium plant, and known as toxic as Illicium anisatum which contains the convulsive sesquiterpene, anisatin, and also the non-toxic compound, pseudoanisatin.[1] We report here the isolation and structure elucidation of majucin (**2**) and neomajucin (**3**), the major constituents of I. majus, which have the same skeleton with anisatin.[2]

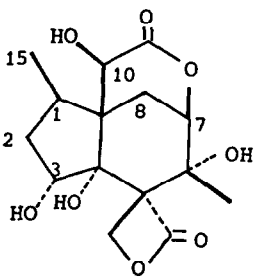
The pericarps(1.5 kg) of I. majus, collected at Guangxi in China, were extracted with methanol. The extract was subjected to the counter current distribution and the chromatographic separation over silica gel successively to give anisatin[3] (**1**)(17 mg) and two new sesquiterpenes, named majucin (**2**)(1.23 g) and neomajucin (**3**)(496 mg).

The major compound, majucin (**2**), colourless needles(from methanol), m.p. 251-252 °C, $[\alpha]_D^{24}$ -74 °(c 0.15, dioxane); m/z 328, was assigned the molecular formula for $C_{15}H_{20}O_8$, the same with that of anisatin. Upon a usual acetylation, (**2**) gave a monoacetate (**4**). The IR spectrum of (**2**) exhibited no β-lactone, but γ- and δ-lactones at 1760 and 1732 cm^{-1} respectively. The ^1H and ^{13}C NMR spectra of (**2**) showed several resemblances to those of (**1**). A doublet methyl at δ_H 1.10 and a singlet methyl at δ_H 1.95, as well as H-10, H-7, and H-3 signals at δ_H 4.65, 5.14, and 5.21 respectively, whose signals are characteristic for the ^1H NMR spectrum of anisatin, could be seen in the ^1H NMR spectrum of (**2**). There is an 8% NOE from the H-15 signal to the H-10 signal indicating that the stereo structures at C-1 and C-10 are the same with those of anisatin. The proton connectivities of H-15(methyl)- H-1- H-2- H-3 and H-7- H-8, revealed by the ^1H-^1H 2D-COSY spectrum, were similar to those of (**1**). The singlet methyl(H-13 or H-14) was weakly coupled with one of the methylene protons of γ-lactone at δ_H 5.11, thus they were correlated with the

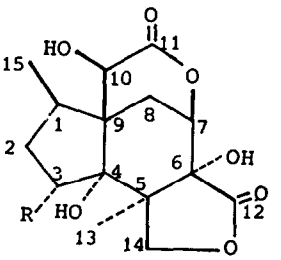
Table 1. ^{13}C NMR data for (1),(2), and (3) (D_5-pyridine,22.5MHz)

C	(1)	(2)	(3)
C-1	37.4 d	38.0 d	39.4 d
C-2	41.9 t	42.9 t	31.4 t
C-3	71.1 d	72.7 d	31.6 t
C-4	85.4 s	82.8 s	84.1 s
C-5	26.0 s	47.5 s	47.5 s
C-6	74.8 s	79.9 s	79.6 s
C-7	81.5 d	80.6 d	80.5 d
C-8	27.5 t	27.1 t	27.5 t
C-9	50.6 s	51.5 s	51.0 s
C-10	70.0 d	70.3 d	70.7 d
C-11	174.6 s	174.7 s	174.8 s
C-12	22.0 q	177.6 s	177.2 s
C-13	168.6 s	20.9 q	21.4 q
C-14	65.2 t	72.4 t	72.6 t
C-15	13.7 q	14.1 q	14.3 q

All assignments were made by the ^{1}H-^{13}C and ^{1}H-^{13}C long-range COSY spectra.



(1) anisatin



(2) R=OH majucin
(3) R=H neomajucin
(4) R=OAc

Table 2. ^{1}H NMR data for (1),(2) and (3) (D_5-pyridine,400MHz)

H	(1)	(2)	(3)
1	2.73 qdd	3.02 qdd	2.90 m
2α	2.37 ddd	2.47 dt	2.39 dt
2β	2.18 ddd	2.21 ddd	2.29 m
3	5.57 dd	5.21 dd	1.85-2.05(2H) m
7	4.44 dd	5.14 dd	5.12 dd
8α	2.04 dd	2.05 dd	2.00 dd
8β	2.73 dd	3.11 dd	3.01 dd
10	4.49 br.d	4.65 br.d	4.66 br.d
10-OH	8.70 br.d	8.95 br.d	8.78 br.d
12	1.79 s	------	------
13	-----	1.95 br.s	1.70 br.s
14a	4.50 d	4.30 d	4.19 d
14b	5.06 d	5.11 br.d	5.02 br.d
15	1.10 d	1.10 d	1.18 d

J(1);(1,15)7.3,(1,2α)12.4,(1,2β)11.0,(2α,2β)14.8,(2α,3)9.5,(2β,3)4.4,(7,8α)3.7,(7,8β)2.0,(8α,8β)14.7,(10,OH)4.4,(14a,14b)6.2 Hz.

J(2);(1.15)7.0,(1,2α)9.5,(1,2β)10.2,(2α,2β)12.6,(2α,3)9.5,(2β,3)4.4,(7,8α)3.3,(7,8β)2.2,(8α,8β)14.3,(10,OH)4.5,(14a,14b)10.8 Hz.

J(3);(7,8α)2.6,(7,8β)2.5,(8α,8β)14.2,(10,OH)4.8,(14a,14b)11.0,(15,1)7.0 Hz.

geminal position at C-5. These evidences were supported by the ^{1}H- ^{13}C long-range 2D-COSY spectrum of (**2**). Therefore, it was suggested that the γ-lactone is formed between the C-12 keto group and the C-13 or C-14 hydroxymethyl group. The structure of (**2**) including the γ-lactone moiety was clarified by an X-ray study of the analogous compound (**3**). Since the shape of H-3 signal in the ^{1}H NMR of (**2**) was not compatible to that of pseudoanisatin(H-3α)[4] but to that of anisatin(H-3 β), (**2**) has a 3 α-hydroxy group.

Neomajucin (**3**), colourless octahedrons(from ethylacetate), m.p. 220-222 °C, $[\alpha]_D^{24}$ -75 °(c 0.25, dioxane); m/z 312. The molecular formula of (**3**), $C_{15}H_{20}O_7$, indicated one oxygen atom less than that of (**2**). (**3**) gave no acetate, upon a usual acetylation. The ^{1}H and ^{13}C NMR spectral data of (**3**) strongly resembled to those of (**2**). The methylene carbon(C-3) appeared in the ^{13}C NMR spectrum of (**3**) instead of one of the hydroxymethine signals in that of (**2**), and the C-3 carbon was revealed to be a methylene carbon by the ^{1}H NMR spectrum of (**3**). Thus, neomajucin (**3**) is the 3-deoxy compound of majucin (**2**).

The structure of (**3**) was confirmed by X-ray diffraction method. Compound (**3**) ($C_{15}H_{20}O_7$) crystallized from ethylacetate in the orthorombic space group $P2_12_12_1$ with a=16.611(2), b=11.985(1), c=6.855(1)Å, and Z=4. All unique diffraction maxima with $2\theta < 128^{\circ}$ were collected on a Rigaku AFC-5R apparatus using a graphite monochromated Cu K α radiation (1.5418 Å) and the θ-2θ scan technique. After correcting for Lorentz and polarization effects, 1300 of the 1318 independent reflections were considered as observed(Fo > 2σ(Fo)). The structure was solved by direct methods with MULTAN84[5] series of program, in which RATAN was used to solve the phase problem. A block-diagonal least-squares refinements with anisotropic nonhydrogen atoms and isotropic hydrogen atoms have lowered the R value to 0.057.[6]

The conformation of the molecule thus obtained is shown in the Figure 1.

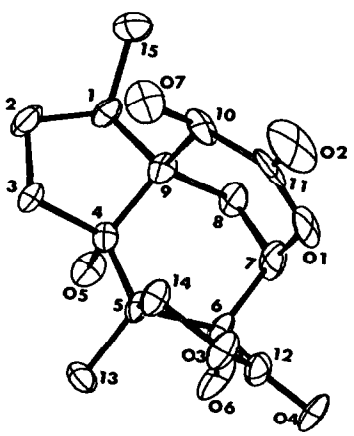


Fig. 1. Molecular conformation and atomic labelling.

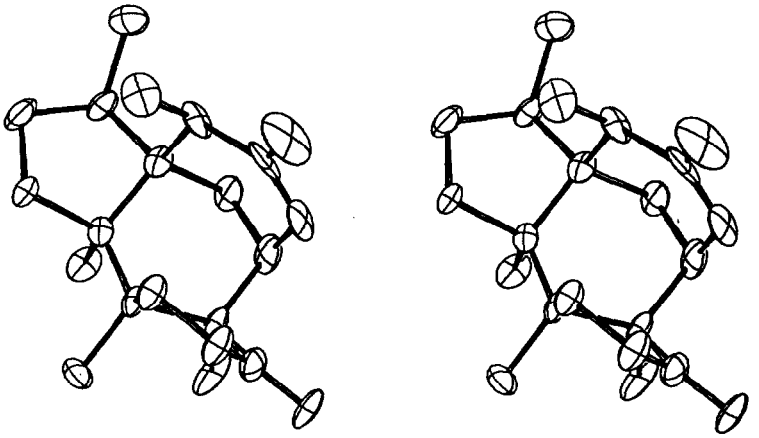


Fig. 2. Stereoscopic drawing of the molecule.

Each toxicity of majucin and neomajucin has been preliminarily examined, and revealed that majucin has no toxicity, but neomajucin exhibited the less toxicity (mouse LD_{50} ca.10 mg/kg), one tenth of that of anisatin.

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6) The atomic coordinates, bond lengths and angles have been deposited with Cambridge Crystallographic Data Center.

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