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STRUCTURE OF ANISLACTONE A; A NEW SKELETAL TYPE OF SESQUITERPENE FROM THE PERICARPS OF *Illicium anisatum*

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Summary: A novel sesquiterpene lactone was isolated from the pericarps of *Illicium anisatum*, a well known toxic plant in Japan, and its structure was established from spectral data and X-ray crystallographic analysis.

Illicium anisatum L. (Illiciaceae) is a toxic tree native to Japan. A unique skeletal sesquiterpene, anisatin,[1,2] was isolated from the fruits (Japanese star anise), and is well known as a potent convulsive constituent. Three other constituents of this type isolated from this plant, neoanisatin,[2] pseudoanisatin,[1,3] and 6-deoxymajucin,[4] have been known so far. Our detailed research on the constituent of the pericarps of *I. anisatum* has led to the isolation of a new skeletal type of compound, named anislactone A (1) (12mg), from the MeOH extract of *I. anisatum* (5.5 kg; dry weight) by a combination of counter-current (EtOAc-H_2O) distribution and silica gel column chromatography ($CHCl_3$-MeOH).

Anislactone A (1) crystallized from $CHCl_3$-EtOAc as colorless prisms, m.p. 274-275°C, $[\alpha]_D$ -47.7°(dioxane, *c* 0.21). The molecular formula of (1) was established as $C_{15}H_{20}O_6$ by the e.i. mass spectrum (m/z:296 $[M^+]$) and ^1H and ^{13}C counts in their n.m.r. spectra. The ^1H n.m.r. spectrum (400MHz, d_5-pyridine) of (1) exhibited three tertiary methyl groups at δ_H1.33, 1.45, and 1.65, together with the signals of AB quartet at δ_H3.36, 3.65 (J=17.2Hz) and δ_H3.99, 4.54 (J=9.9Hz), respectively, clarified by ^1H-^1H two dimensional correlation spectroscopy (2D COSY), and an isolated methine signal at δ_H4.65. Three signals derived from methyl groups were observed in its ^{13}C n.m.r. spectrum (the properties of carbon signals were determined by DEPT), which also showed the signals due to a methine carbon, and four methylene carbons, and five quaternary carbons, along with two lactone carbonyl carbon signals.(Table 1) In the i.r. spectrum (nujol) of (1), the absorptions due to these lactone moieties appeared at 1735 and 1728 cm^{-1}. Both of these lactone rings were revealed to be γ-lactones by analysis of the connectivities in the ^1H-^{13}C long-range 2D COSY of (1). While the presence of two hydroxyl groups were suggested by the carbon signals at δ_C72.7 and 88.4, (1) gave a mono acetylated compound (δ_H2.15 AcO-) under a forcing condition (DMAP-pyridine-Ac_2O), which suggested one is tertiary, and another is a sterically hindered hydroxyl group. These spectral and chemical results enabled some structural features of (1) to be deduced. However, the whole structure including the relative stereochemistry could not be clarified. The complete structure and stereochemistry of (1) were confirmed by single-crystal X-ray analysis.

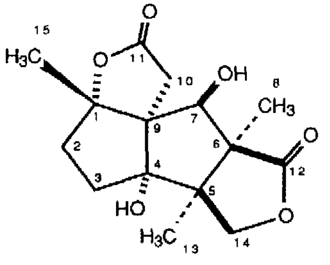
Anislactone A (1) forms colorless prisms from $CHCl_3$-EtOAc, orthorhombic, space group $P2_12_12_1$, a=22.095(7), b=8.938(2), c=7.407(2)Å (from 20 orientation reflections: 30°<2θ<50°), U=1462.8$Å^3$, and Z=4, D_c=1.35gcm^{-1}. Intensity data(2θ<128°, 1431 reflections) were obtained on a Rigaku AFC-5R diffractometer (graphite-monochromatized Cu Kα radiation; 2θ-θ scans), yielded 1406 reflections [Fo>2σ(Fo)] which were used for the structure analysis. All intensities were corrected for Lorentz and polarization effects but not for absorption. The

Table 1. ^{1}H and ^{13}C n.m.r. data for anislactone A (δ: in d_5-pyridine)†

position	^{1}H(400MHz)	^{13}C(100MHz)
1	—	95.9 s
2a	2.40(dd,J=13.6,7.2)	37.8 t
2b		
3	2.03-2.17(m,3H)	36.3 t
4	—	88.4 s
5	—	55.4 s*
6	—	57.6 s*
7	4.65 s	72.7 d
8	1.45 s	11.9 q
9	—	68.3 s
10a	3.65(d,J=17.2)	31.7 t
10b	3.36(d,J=17.2)	
11	—	176.8 s
12	—	181.0 s
13	1.33 s	17.8 q
14a	4.54(d,J=9.9)	73.7 t
14b	3.99(d,J=9.9)	
15	1.65 s	21.1 q

* Assignments may be interchanged.

† Assignments were made on the basis of 2D ^{1}H-^{13}C COSY and 2D ^{1}H-^{13}C long-range COSY spectra.



(1) anislactone A

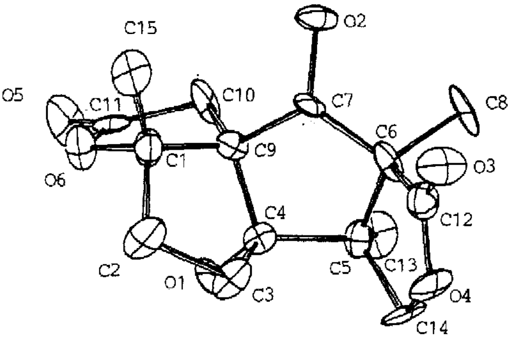


Figure 1. ORTEP view of the structure of (1)

crystal structure was solved by direct methods using the MULTAN84 series of programs, with RATAN being used to obtain the phases and refined by block-diagonal least-squares methods. The final refinements with anisotropic temperature factors for the non-hydrogen atoms and isotropic temperature factors for hydrogen atoms were lowered *R* value to 0.054. (Figure 1)

Considering from the X-ray structure of (1), compound (1) may be biogenetically correlated with majucin[5] and/or anisatin, thus the systematic numbering for anislactone A was temporarily based on that of majucin. Much attention should be focused on an inversion of the configuration at C-9 from that of the usual anisatin-type structure.

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