Chem. Pharm. Bull.
28(6)1951—1954(1980)

Novel Phytoquinoids from *Illicium tashiroi* Maxim.

Four new phytoquinoids, illicinone-A, -B, -C, and -D were isolated from the leaves of *Illicium tashiroi* Maxim., and their structures were determined to be **1**, **2**, **3**, and **4**, respectively, by spectral and chemical evidences.

Keywords——phytoquinoid; illicinone-A; illicinone-B; illicinone-C; illicinone-D; 1,4-dien-3-one; *Illicium tashiroi* Maxim.; Magnoliaceae; CMR; thermal rearrangement

Phytoquinoids are known only few examples occurring in higher plants, and are of interest in exhibiting both antitumor and cytotoxic activities.[1] We wish to report the isolation and structure elucidations of novel four phytoquinoids from leaves of *Illicium tashiroi* Maxim. (Japanese name, Yaeyamashikimi) (Magnoliaceae) collected on Iriomote island.[2]

Chloroform extract of the dried leaves of the plant was chromatographed on silica gel, and eluted with benzene, chloroform, and chloroform–methanol (10: 1), successively. And each fraction was furnished with preparative silica gel thin-layer chromatography, and isolated some allyl- and/or prenyl-aromatic compounds[3] and four phytoquinoids, named illicinone-A, -B, -C, and -D.

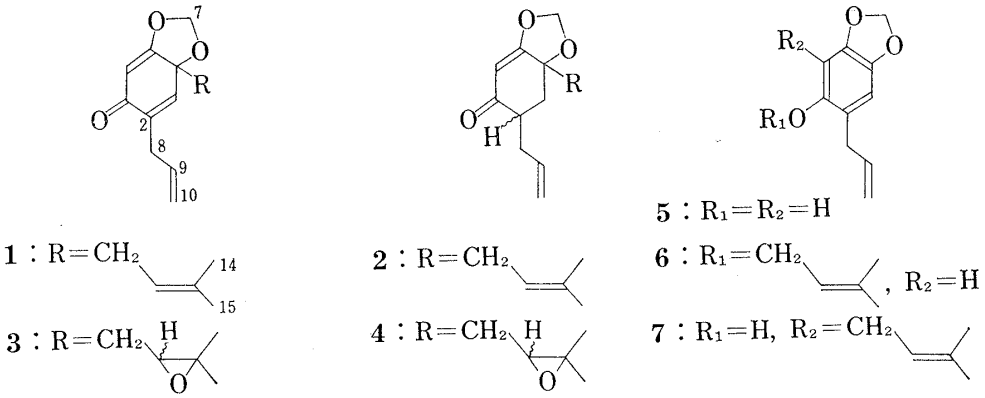

Chart 1

Illicinone-A, colorless oil, $C_{15}H_{18}O_3$. MS *m/e* (relative intensity): 246 (M^+, 12), 178 (100), 151 (41), 147 (64), 119 (39). $[\alpha]_D$ +101° ($CHCl_3$). The proton magnetic resonance (PMR) spectrum (Table I) and carbon-13 magnetic resonance (CMR) spectrum (Table II) showed the presence of an allyl and a prenyl group in illicinone-A. The bands at 1665, 1630, and 1610 cm^{-1} in infrared absorption (IR) spectrum could be assigned to a *p*-quinoid type system, and this was supported with the ultraviolet absorption (UV) spectrum (λ_{max}^{EtOH} nm: 207, 237, 283). In the PMR spectrum of illicinone-A, lower field one-proton singlet at δ 6.54 having long range coupling, and another one-proton sharp singlet at δ 5.47—5.56 region[4] were assigned with olefinic protons attached at β- and α-carbons in the 1,4-dien-3-one system, respectively. The characteristic two singlets at δ 5.47—5.56 region[4] in PMR spectrum, and a triplet at δ 97.9

1) S.R. Jensen, A. Kjaer, and B.J. Nielsen, *Acta Chem. Scand.*, **27**, 367 (1973); M. Ogura, G.A. Cordell, and N.R. Farnsworth, *J. Natur. Prod.*, **39**, 255 (1976); *idem*, *ibid.*, **40**, 157 (1977).
2) Several phenolic compounds from the leaves of *Illicium anisatum* L. (Japanese name, Shikimi) have been isolated previously: M. Shibuya, K. Abe, Y. Nakahashi, and S. Kubota, *Chem. Pharm. Bull.*, **26**, 2671 (1978).
3) Isolations and characterisations of these compounds will be reported elsewhere.
4) Three one-proton sharp singlets (δ 5.47, 5.54, and 5.56) were appeared in this region, and the accurate assignment was difficult; G. Büchi, P. Chu, A. Hoppmann, C. Mak, and A. Pearce, *J. Org. Chem.*, **43**, 3983 (1978).

in CMR spectrum show the presence of a methylenedioxy moiety in the molecule.[5] The appearance of the base fragment peak at *m/e* 178 due to the elimination of the prenyl moiety from the molecular ion in the MS spectrum of illicinone-A indicated that the prenyl group attached at the allylic carbon at C-4.

Considerations from these results together with the CMR spectral data (Table II) led to the plane structure **1** for illicinone-A.

Table I. PMR Spectral Data for Illicinone-A, -B, -C, and -D (in $CDCl_3$)

Proton No.	Chemical shift (ppm)			
	Illicinone-A	Illicinone-B	Illicinone-C	Illicinone-D
C_2–H	—	*	—	*
C_3–H	6.54(s)	*	6.79(s)	*
$C_{6,7}$–H	5.47(s)	5.35(s)	5.55(2H, s)	5.36(s)
	5.54(s)	5.43(s)	5.63(s)	5.49(s)
	5.56(s)	5.49(s)		5.58(s)
C_8–H	3.01(d) J=7	*	3.07(d) J=7	*
C_9–H	5.78(m)	5.66(m)	5.84(m)	5.72(m)
C_{10}–H	5.02(m)	5.01(m)	5.09(m)	5.03(m)
C_{11}–H	2.43(brd) J=7	*	1.73(dd) J=8, 15	1.56(dd) J=9, 15
			2.24(dd) J=5, 15	
C_{12}–H	4.95(m)	5.13(m)	2.80(dd) J=5, 8	2.93(dd) J=3, 9
$C_{14,15}$–H	1.54(s)	1.64(s)	1.23(s)	1.28(s)
	1.68(s)	1.76(s)	1.30(s)	1.36(s)

* These signals could not be assigned because of overlapping with other signals; (illicinone-B: 2.15—2.76 ppm, illicinone-D: 2.20—2.80 ppm).
(s): singlet, (d): doublet, (brd): broad doublet, (dd): double doublets, (m): multiplet.

Table II. CMR Spectral Data for Illicinone-A, -B, -C, and -D (in $CDCl_3$)

Carbon No.	Chemical shift (ppm)			
	Illicinone-A	Illicinone-B	Illicinone-C	Illicinone-D
1	186.2	197.9	186.2	198.0
2	139.0	42.0	138.8	41.7
3	134.1	30.4	134.2[b]	31.2
4	81.9	82.6	80.0	81.9
5	173.3	175.5	173.4	175.0
6	98.0	98.7	98.3	99.0
7	97.9	97.3	97.9	97.2
8	33.3	35.3[a]	33.3	35.2[c]
9	134.6	135.2	134.4[b]	135.0
10	116.8	117.1	117.3	117.1
11	34.7	35.5[a]	36.3	35.5[c]
12	115.8	116.5	58.9	59.1
13	137.1	136.2	58.1	57.1
14	17.8	18.1	18.8	19.0
15	25.7	25.9	24.5	24.6

Values with the same superscript could be interchanged. The assignment was established by the off-resonance and selective decoupling techniques.

5) The assignment of this signal was established by the off-resonance and the gated decoupling techniques.

Further evidences for the establishment of structure **1** for illicinone-A were provided by follows: Thermal treatment of illicinone-A at 190—200° in sealed tube yielded three aromatized rearrangement products **5**, **6**,[6] and **7** in 31, 13, and 11% yield, respectively, which were characterized with the PMR, CMR, and MS spectra.[7] Furthermore, illicinone-A can be obtained from the reaction of **5** with dimethylallyl bromide in the presence of NaH in DMF in 3% yield along with **6** as major product (65% yield).

On the basis of these results, illicinone-A should be represented by the formula **1**.[8]

Illicinone-C, colorless oil, $C_{15}H_{18}O_4$. MS *m/e* (relative intensity): 262 (M^+, 14), 178 (45), 162 (43), 147 (100), 119 (45). $[\alpha]_D$ +128° ($CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1670, 1635, 1615. UV λ_{max}^{EtOH} nm: 206, 241, 289. The IR and UV spectra show the presence of the *p*-quinoid structure as the same with **1**. The PMR spectrum of illicinone-C exhibited, instead of the olefinic proton signal at δ 4.94 and methylene protons signal at δ 2.43 due to a prenyl moiety as seen in **1**, a new ABC type signals at δ 1.72 (dd, J=8, 15 Hz), 2.24 (dd, J=5, 15 Hz), and 2.80 (dd, J=5, 8 Hz). Other PMR signals as shown in Table I are nearly identical in form and multiplicity with the signals for the corresponding groups of **1**. Furthermore, in the comparison of CMR spectra of **1** and illicinone-C, a doublet at δ 115.8 and a singlet at δ 137.1 in **1** were observed to upfield shift at δ 58.9 (d) and δ 58.1 (s) in illicinone-C, respectively. These data show the presence of the epoxygenated prenyl moiety in the molecule of illicinone-C, instead of the prenyl group in **1**. The MS spectrum of illicinone-C also supported the fact that the fragment peak at *m/e* 178, elimination of epoxygenated prenyl moiety from the molecular ion, was appeared, and the fragment pattern was similar with that of the MS spectrum of **1**. The structure of illicinone-C can thus be assigned to formula **3**.

Illicinone-B, colorless oil, $C_{15}H_{20}O_3$. MS *m/e* (relative intensity): 248 (M^+, 37), 180 (100), 178 (42), 149 (66), 139 (72), 137 (84), 121 (28). $[\alpha]_D$ +140° ($CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1630. UV λ_{max}^{EtOH} nm: 205, 249, 278 (sh.). In the PMR spectrum of illicinone-B, disappearance of the characteristic low-field signal at δ 6.54 in **1** was observed, and unresolved overlapping multiplets at the range from δ 2.1 to 2.8 newly appeared. Furthermore, in the CMR spectrum, a triplet at δ 30.4 and a doublet at δ 42.0 were appeared instead of a doublet at δ 134.1 and a singlet at δ 139.0 due to the carbons at C-3 and C-2 in **1**. Other signals in PMR and CMR spectra of illicinone-B were almost identical with these of **1** (Table I and II). These spectral data coupled with the presence of only one absorption band at 1630 cm^{-1} in the carbonyl region suggested the structure of illicinone-B as formula **2** corresponding to 2,3-dihydro derivative of illicinone-A (**1**).

Illicinone-D, colorless oil, $C_{15}H_{20}O_4$. MS *m/e* (relative intensity): 264 (M^+, 12), 196 (11), 178 (37), 163 (18), 149 (15), 137 (15), 125 (100). $[\alpha]_D$ +342° ($CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1635. UV λ_{max}^{EtOH} nm: 205, 248. All pertinent PMR and CMR signals of **2** and illicinone-D, except the signals of prenyl moiety were closely comparable as shown in Table I and II. Newly appearance of the signals at δ 2.93 (1H, dd, J=3, 9 Hz), and 1.56 (1H, dd, J=9, 15 Hz) could be assigned with a part of ABC type signals of C-11 and C-12 protons. Furthermore, in the CMR spectrum of illicinone-D, a singlet at δ 57.1 and a doublet at δ 59.1 were observed instead of the signals at δ 116.5 (s) and 136.2 (d) in the spectrum of **2**. These relationship between **2** and illicinone-D in the spectral data were the same as these between **1** and **3**. The structure **4** was proposed for illicinone-D.

---

6) The compound **6** was also isolated from the same plant source, and named illicinol; [PMR ($CDCl_3$) δ: 1.72, 1.77 (2×3H, 2×s), 3.28 (2H, d, J=7 Hz), 4.42 (2H, d, J=7 Hz), 4.99 (2H, m), 5.43 (1H, t), 5.84 (2H, s), 5.96 (1H, m), 6.49 (1H, s), 6.60 (1H, s)].

7) The same thermal treatment of **6** only afforded with **5** and **7**, and not led to the Claisen type rearrangement products.

8) The determination of the absolute configuration is now in progress.

Faculty of Pharmacy
Meijo University
Yagoto, Tempaku, Nagoya, 468, Japan

KENICHI YAKUSHIJIN
JUNKO SEKIKAWA
RIKA SUZUKI
TAKAYUKI MORISHITA
HIROSHI FURUKAWA
HIROYUKI MURATA

12-cho, Ibusuki, Kagoshima, 891-04, Japan

Received March 28, 1980

[Chem. Pharm. Bull. 28(6)1954—1958(1980)]

Antitumor Active Glycosides from Condurango Cortex

Antitumor active condurangoglycosides A_0 and C_0 were isolated from Condurango Cortex. Their structures were established by chemical and spectral evidences.

Keywords——*Marsdenia cundurango*; Asclepiadaceae; pregnane; ester glycoside; condurangoglycosides A_0 and C_0, antitumor activity; ^{13}C-NMR

The crude drug Condurango Cortex, bark of *Marsdenia cundurango* REICH. (Asclepiadaceae) native to north-western part of South America, has been used as an aromatic bitter stomachic in popular medicine, and also used against cancer or syphylis in folk remedy though no report has been found on such effects.[1] According to the reports on the antitumor screening by CCNSC, the extract of this plant was evaluated failure against Sarcoma-180, Adenocarcinoma 755, Humansarcoma HSl, and KB systems.[2]

Ahsan *et al.* reported that a polyoxypregnane glycoside, amplexoside-A, from a Asclepiadaceae plant *Asclepias amplexicaulis* showed a cancer inhibitory activity in the KB assay.[3] Generally, Asclepiadaceae plant is abundant in the esterified polyoxypregnane glycosides,[4] which therefore, promise sources for anti-tumor agents.

On the constituents of cortex condurango, Tschesche and his co-workers studied the structures of condurango glycosides A (**3**), A_1 (**4**), C (**5**), and C_1 (**6**).[5] We wish to describe in this paper that the separation and structural determinations of two new condurangoglycosides A_0 (**1**) and C_0 (**2**) from the anti-tumor active points of view.

The crude glycoside mixture of condurango obtained by a usual procedure was separated into three fractions using a silica gel column chromatography. One of the fractions which still consisted of at least eight compounds by a high performance liquid chromatography (HPLC) examination showed a strong activity against a solid type Ehrlich carcinoma.[6] The two new glycosides A_0 (**1**) and C_0 (**2**) were obtained from this fraction by a combined HPLC system (Waters prep-500 on silica gel followed by semi preparative scale columns of Wako-gel LC5H and Merck Lichroprep. RP-8).

1) *United States Dispensary*, **25**, 1644 (1955).
2) B.J. Abott, J. Leiter, J.L. Hartwell, M.E. Caldwell, and S.A. Schepartz, *Cancer Research*, **26**, 587 (1966).
3) A.M. Ahsan, D.M. Piatak, and P.D. Sorensen, *Experientia*, **29**, 788 (1973).
4) T. Reichstein, *Naturwissenschaften*, **54**, 53 (1967).
5) *a*) R. Tschesche, M. Baumgarth, and P. Welzel, *Tetrahedron*, **23**, 249 (1967); *b*) T. Tschesche and H. Kohl *ibid.*, **24**, 4359 (1968).
6) Y. Egashira, K. Takano, M. Yamada, Y. Hirokawa, D. Mizuno, M. Abe, and Y. Masamune, *Japan J. Med. Sci. and Biol.*, **12**, 463 (1959).