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Studies on the Constituents of the Plants of *Illicium* Species. II.[1] Structures of Phenolic Components

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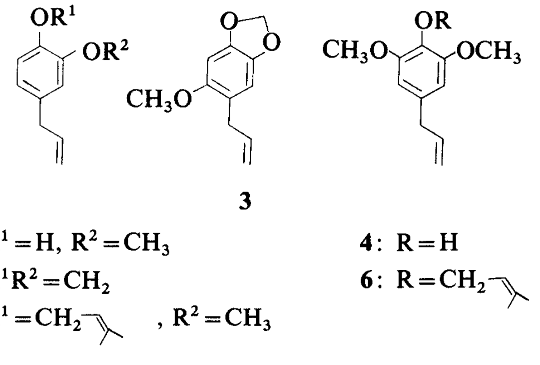
Ten phenolic compounds were isolated from leaves or timber of Illiciaceous plants, *Illicium tashiroi* Maxim., *I. arborescens* Hayata, and *I. anisatum* L., and their structures were determined **1**—**10** by spectroscopic and synthetic studies. Of the ten, 4-allyl-5-(3-methylbut-2-enyloxy)-1,2-methylenedioxybenzene (**7**), 4-allyl-2-methoxy-6-(3-methyl-2-butenyl)phenol (**9**), and 4-allyl-2,6-dimethoxy-3-(3-methyl-2-butenyl)phenol (**10**) are new compounds.

Keywords——phenolic compound; *Illicium tashiroi*; *Illicium arborescens*; *Illicium anisatum*; Illiciaceae; ^{13}C-NMR

Anethole, eugenol (**1**), and safrole (**2**) were isolated from the leaves of *Illicium anisatum* L. (Japanese name, "Shikimi") (Illiciaceae) long ago.[2] Shibuya *et al.*[3] recently reported the isolation of four phenolic components **3**—**6** from the leaves of this plant. We wish to report the isolation and characterization of ten phenolic compounds **1**—**10** from leaves or timber of *I. tashiroi* Maxim. (Japanese name, "Yaeyama-shikimi"), *I. arborescens* Hayata (Japanese name, "Akabana-shikimi"), and *I. anisatum* L., three of these components, 4-allyl-5-(3-methylbut-2-enyloxy)-1,2-methylenedioxybenzene (illicinole) (**7**), 4-allyl-2-methoxy-6-(3-methyl-2-butenyl)phenol (**9**), and 4-allyl-2,6-dimethoxy-3-(3-methyl-2-butenyl)phenol (**10**), being new compounds.



3

1: R^1=H, R^2=CH$_3$

2: R^{1}R^2=CH$_2$

5: R^1=CH$_2$, R^2=CH$_3$

4: R=H

6: R=CH$_2$

Chart 1

Phenolic Components from Leaves of *I. tashiroi* Maxim.

Chloroform extract of the dried leaves of this plant was chromatographed on silica gel, and eluted with benzene, chloroform, and chloroform–methanol (10 : 1) successively.[1] The benzene fraction was subjected to preparative silica gel layer chromatography to give three oily compounds. One of them was shown to be a new compound, and was named illicinole.

The molecular weight of illicinole was found to be 246 from the parent ion peak in the mass spectrum. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum showed the presence of two aromatic protons at δ 6.60 and 6.48, a methylenedioxy group at δ 5.85, an allyl group and a prenyl group. Two doublets ($J = 6$ Hz) due to methylenes of the allyl group and the prenyl group appeared at δ 4.41 and 3.28, and the lower field signal was coupled with the triplet (δ 5.43, $J = 6$ Hz) attributable to the olefinic proton of the prenyl group. Further, long-range coupling was observed in the higher field methylene doublet. On the basis of these results, illicinole was assigned as 4-allyl-5-(3-methylbut-2-enyloxy)-1,2-methylenedioxybenzene (**7**). This assignment was confirmed by direct comparison of illicinole with an authentic sample **7** obtained by the reaction of 2-allyl-4,5-methylenedioxyphenol (**11**)4) and prenyl bromide.5) In this reaction, 6-allyl-6-(3-methyl-2-butenyl)-3,4-methylenedioxycyclohexa-2,4-dienone (**12**)6) and illicinone-A (**13**)7) were also obtained as minor products.

The structures of the other two compounds were confirmed by direct comparison with commercial safrole (**2**) and 1-allyl-3-methoxy-4-(3-methylbut-2-enyloxy)benzene (**5**)3) synthesized by the reaction of eugenol (**1**) with prenyl bromide.

Phenolic Component from Leaves of *I. arborescens* Hayata

Illicinole (**7**) was the only phenolic component isolated from the chloroform extract of the dried leaves of this plant.1)

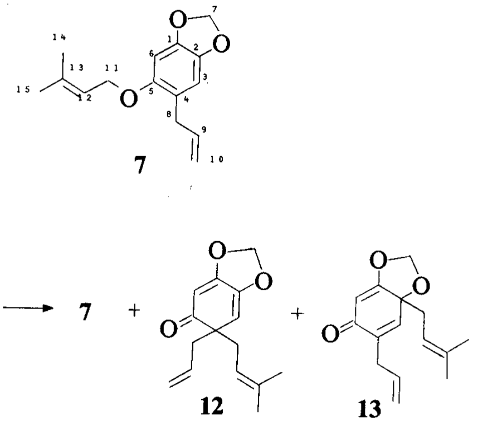


Chart 2

Phenolic Components from Leaves of *I. anisatum* L.

Chloroform extract of the fresh leaves of this plant was chromatographed on silica gel and the products were purified by preparative silica gel layer chromatography to give six oily compounds. The structures of two (compounds A and B) of them were confirmed as follows. The ^{1}H-NMR spectrum of compound A indicated the presence of a methoxy group (δ 3.90), a methylenedioxy group (δ 5.95), two aromatic protons (δ 6.41 and 6.38) and an allyl group. Consideration of these ^{1}H-NMR signals and the parent ion peak at *m/e* 192 in the mass spectrum (MS) led us to assign the structure of compound A as 1-allyl-3-methoxy-4,5-methylenedioxybenzene (**8**). This compound was identical with a sample prepared by the method of Trikojus *et al.*9) The isolation of **8** from a natural source10) has been reported, but this is the first isolation from *I. anisatum* L.

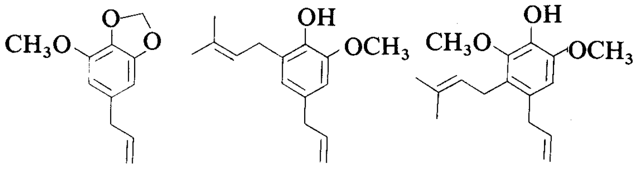
The infrared (IR) spectrum of compound B showed absorption at 3525 cm^{-1} attributable to a hydroxy group, and its molecular weight was found to be 232 from the mass spectrum. The ^{1}H-NMR spectrum ($CDCl_3$) indicated the presence of a methoxy group (δ 3.88), two aromatic protons (δ 6.57), an allyl group, a prenyl group and a proton (δ 5.56) exchangeable with deuterium oxide. Two aromatic protons were observed as mutually *meta*-coupled doublets ($J = 2$ Hz) at δ 6.69 and 6.58 in the ^{1}H-NMR spectrum (acetone-d_6). From these data, the structure of compound B was assigned as 4-allyl-2-methoxy-6-(3-methyl-2-butenyl)phenol (**9**). This assignment was supported by the identification of **9** with the product obtained, along with **1**, from thermal reaction of **5**.

The other compounds were confirmed to be eugenol (**1**), 1-alllyl-2-methoxy-4,5-methylenedioxybenzene (**3**),[8] **5** and 1-allyl-3,5-dimethoxy-4-(3-methylbut-2-enyloxy)benzene (**6**) by direct comparison with a commercial sample or authentic samples synthesized by the reported methods.[3,4]

Phenolic Components from Timber of *I. anisatum* L.

Chloroform extract of the fresh timber of this plant afforded five oily compounds as phenolic components. The structures of four compounds were easily confirmed by direct comparison with **3**, 4-allyl-2,6-dimethoxyphenol (**4**),[11] **6** and **8**.

The ^{1}H-NMR spectrum of the other compound showed signals assignable to an aromatic proton (δ 6.52), two methoxy groups (δ 3.86 and 3.84), an allyl group and a prenyl group. The mass spectrum showed the parent ion peak at 262 and the IR spectrum showed the absorption of a hydroxy group at 3535 cm^{-1}. From these spectral data and comparison of the ^{13}C-NMR spectrum with those of other known substances, as shown in Table I, the structure was considered to be 4-allyl-2,6-dimethoxy-3-(3-methyl-2-butenyl)phenol (**10**).[13]



8 **9** **10**

Chart 3

Table I. ^{13}C-NMR Spectral Data for Natural Products **1**—**10** and Synthetic Compounds **11** and **12**[a]

	1[12]	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
1	144.1	145.5	146.0	130.8	149.2	135.3	145.8	134.3	141.3	128.8	148.2	163.6
2	146.8	147.3	140.7	146.7	146.4	153.3	140.9	148.6	145.9	145.3	141.2	143.7
3	111.5	107.9	109.4	105.0	112.0	105.4	109.2	102.5	108.5	126.0	109.3	108.6
4	131.9	133.5	120.6	132.8	132.5	135.3	121.3	134.3	130.7	130.7	116.7	54.0
5	121.3	121.0	151.8	105.0	120.1	105.4	150.9	107.6	122.2	107.8	148.2	201.9
6	114.7	108.8	94.7	146.7	113.3	153.3	96.4	143.2	126.8	145.3	98.4	99.4
7		100.5	100.7				100.7	101.0			100.7	101.0
8		39.8	33.9	40.2	39.7	40.5	34.0	40.1	39.9	36.9	34.9	44.6
9		137.3	137.0	137.3	137.4	137.0	137.0	137.0	137.7	137.2	136.2	132.8
10		115.3	114.9	115.4	115.3	115.6	114.9	115.6	115.1	115.1	116.0	117.8
11					65.9	69.3	66.6		28.2	25.0		39.2
12					120.1	120.9	120.0		121.5	123.5		118.2
13					136.9	137.1	137.0		132.1	136.7		134.5
14					18.1	17.8	18.2		17.8	17.9		18.0
15					25.7	25.7	25.7		25.7	25.6		25.8
			56.4	56.1 ×2	55.7	55.9 ×2		56.4	55.9	60.5 56.0		

[a] The numbering system of 7 was selected to facilitate comparison of analogous carbons.

Experimental

IR spectra were recorded on a Jasco IR-A-1 spectrometer. ^{1}H- and ^{13}C-NMR spectra were taken on JEOL PX-100 and/or JEOL FX-100 spectrometers with tetramethylsilane as an internal standard. Abbreviations used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. MS were recorded on a Hitachi M-52 spectrometer operating at an ionization potential of 70 eV. Column chromatography was performed with Kieselgel 60 (70—230 mesh, Merck). Preparative layer chromatography (PLC) was carried out on plates (20 × 20 cm, 0.75 mm in thickness) coated with Kieselgel PF_{254} (Merck).

Plant Materials——*Illicium tashiroi* MAXIM., *I. arborescens* HAYATA, and *I. anisatum* L. were collected on Iriomote Island (Japan), Nanjenshan, Pingtung (Taiwan), and Mie Prefecture (Japan), respctively. The leaves of *I. tashiroi* and *I. arborescens* were dried before use at room temperature and in a drying oven at 45 °C, respectively.

Extraction and Separation——The leaves or timber of *Illicium* species were extracted with $CHCl_3$ (10 1 × 4) at room temperature. The extract was concentrated under reduced pressure at 30—35 °C. The residue was chromatographed on a column (100 × 6 cm) of silica gel (75 cm) with benzene, $CHCl_3$ and $CHCl_3$–MeOH (10 : 1) successively,[1] and the products were purified by PLC [hexane–ether (9 : 1), benzene or benzene–hexane (5 : 1)].

Phenolic Components of the Leaves of *I. tashiroi* MAXIM.——Three compounds, **2** (150 mg), **5** (130 mg) and **7** (300 mg) were obtained from the dried leaves (350 g) of this plant. **2** was identical with commercial safrole on the basis of IR ($CHCl_3$) and ^{1}H-NMR ($CDCl_3$) spectral comparisons.

1-Allyl-3-methoxy-4-(3-methylbut-2-enyloxy)benzene (5)——Colorless oil. IR ν_{max} ($CHCl_3$): 1675 (R–CH=CR′R″), 1640 (–CH=CH$_2$) cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 6.78 (1H, d, J=8 Hz), 6.66 (1H, s), 6.64 (1H, d, J=8 Hz), 5.92 (1H, m), 5.48 (1H, br t, J=6 Hz), 5.01 (2H, m), 4.52 (2H, br d, J=6 Hz), 3.82 (3H, s), 3.30 (2H, br d, J=6 Hz), 1.76, 1.72 (each 3H, s). MS *m/e*: 232 (M$^+$), 164, 149, 131, 121, 103, 91. This compound was shown to be identical with **5** prepared by the reaction of eugenol (**1**) and prenyl bromide.[3]

Illicinole (4-Allyl-5-(3-methylbut-2-enyloxy)-1,2-methylenedioxybenzene) (7)——Colorless oil. IR ν_{max} ($CHCl_3$): 1638 (–CH=CH$_2$), 938 (–OCH$_2$O–) cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 6.60 (1H, s), 6.48 (1H, s), 5.91 (1H, m), 5.85 (2H, s), 5.43 (1H, br t, J=6 Hz), 4.99 (2H, m), 4.41 (2H, br d, J=6 Hz), 3.28 (2H, br d, J=6 Hz), 1.77, 1.72 (each 3H, s). MS *m/e* 246 (M$^+$), 178, 162, 151, 147, 119, 91. UV λ_{max} (EtOH) (ε): 210 (15700), 240 (6500), 302 (6200) nm.

Reaction of 2-Allyl-4,5-methylenedioxyphenol (11) with Prenyl Bromide——A mixture of **11**[4] (1 g) and 50% NaH (0.3 g) washed with petroleum ether in dimethylformamide (DMF) (5 ml) was cooled to 0—5 °C, and prenyl bromide (0.9 g) was added to the mixture with stirring. After half an hour, the reaction mixture was poured onto ice-water and extracted with ether. Ether extract was dried over $MgSO_4$ and concentrated. The residue was purified by PLC ($CHCl_3$) to give **7** (65%), **12** (15%) and **13** (3%). The product **7** was shown to be identical with illicinole by IR and ^{1}H-NMR spectral comparisons. 6-Allyl-6-(3-methyl-2-butenyl)-3,4-methylenedioxycyclohexa-2,4-dienone (**12**): Colorless oil. IR ν_{max} ($CHCl_3$): 1613 (C=O) cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 5.80 (2H, s), 5.57 (1H, s), 5.51 (1H, m), 5.39 (1H, s), 4.98 (3H, m), 2.70—2.10 (4H, m), 1.64, 1.59 (each 3H, s). MS *m/e*: 246 (M$^+$), 189, 178, 151, 147, 133, 119, 91. UV λ_{max} (EtOH) (ε): 212 (11230), 247 (6800), 309 (3400) nm. The product **13** was shown to be identical with illicinone-A[7] by IR and ^{1}H-NMR spectral comparisons.

Phenolic Component of the Leaves of *I. arborescens* HAYATA——Illicinole (**7**) (200 mg) was obtained from the dried leaves (500 g) of this plant.

Phenolic Components of the Leaves of *I. anisatum* L.——Six compounds, **1** (7 mg), **3** (350 mg), **5** (250 mg), **6** (200 mg), **8** (25 mg) and **9** (25 mg), were obtained from the fresh leaves (2 kg) of this plant. **1** and **5** were shown to be identical with commerical eugenol and 1-allyl-3-methoxy-4-(3-methylbut-2-enyloxy)benzene, respectively, by IR and ^{1}H-NMR spectral comparisons.

1-Allyl-2-methoxy-4,5-methylenedioxybenzene (3)——Colorless oil. IR ν_{max} ($CHCl_3$): 1635 (–CH=CH$_2$), 932 (–OCH$_2$O–) cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 6.64 (1H, s), 6.51 (1H, s), 5.94 (1H, m), 5.86 (2H, s), 5.01 (2H, m), 3.73 (3H, s), 3.28 (2H, br d, J=6 Hz). MS *m/e* 192 (M$^+$), 165, 147, 119, 91. This compound was shown to be identical with **3** prepared by Alexander *et al.*[4] (IR and ^{1}H-NMR spectra).

1-Allyl-3,5-dimethoxy-4-(3-methylbut-2-enyloxy)benzene (6)——Colorless oil. IR ν_{max} ($CHCl_3$): 1635 (–CH=CH$_2$) cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 6.32 (2H, s), 5.88 (1H, m), 5.52 (1H, br t, J=6 Hz), 5.03 (2H, m), 4.40 (2H, br d, J=6 Hz), 3.78 (6H, s), 3.27 (2H, br d, J=6 Hz), 1.73, 1.64 (each 3H, s). This compound was shown to be identical with **6** prepared by Shibuya *et al.*[3] (IR and ^{1}H-NMR spectra).

Compound A (5-Allyl-1-methoxy-2,3-methylenedioxybenzene) (8)——Colorless oil. IR ν_{max} ($CHCl_3$): 1630 (–CH=CH$_2$), 935 (–OCH$_2$O–) cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 6.41 (1H, br s), 6.38 (1H, br s), 5.95 (2H, s), 5.96 (1H, m), 5.08 (2H, m), 3.90 (3H, s), 3.31 (2H, br d, J=6 Hz). MS *m/e*: 192 (M$^+$), 161, 147, 131, 119, 91. This compound was shown to be identical with **8** prepared by Trikojus *et al.*[9] (IR and ^{1}H-NMR spectra).

Compound B (4-Allyl-2-methoxy-6-(3-methyl-2-butenyl)phenol) (9)——Colorless oil. IR ν_{max} ($CHCl_3$): 3525 (OH), 1630 (–CH=CH$_2$) cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 6.57 (2H, s), 5.96 (1H, m), 5.56 (1H, s, OH), 5.34 (1H, br t, J=6 Hz), 5.08 (2H, m), 3.88 (3H, s), 3.34 (4H, m), 1.76 (6H, s). ^{1}H-NMR δ (CD_3COCD_3) 7.17 (1H, s, OH), 6.69 (1H, br d, J=2 Hz), 6.58 (1H, br d, J=2 Hz), 5.95 (1H, m), 5.33 (1H, br t), 5.06 (2H, m), 3.82 (3H, s), 3.31 (4H, m), 1.73 (6H, s). MS *m/e*: 232 (M$^+$), 191, 177, 151, 147, 131, 115, 91.

Thermal Reaction of 5——A solution of **5** (0.2 g) in DMF (2 ml) was heated in a sealed tube at 190—200 °C for 4 h. The reaction mixture was poured into water and extracted with ether. The ether extract was dried over $MgSO_4$ and concentrated. The residue was purified by PLC ($CHCl_3$) to give **1** (70 mg) and **9** (25 mg). **9** was shown to be identical with compound B from a natural source.

Phenolic Components of Timber of *I. anisatum* L.——Five compounds, **3** (290 mg), **4** (35 mg), **6** (70 mg), **8** (20 mg) and **10** (20 mg), were obtained from fresh timber (1 kg) of this plant. **3**, **4**, **6**, and **8** were shown to be identical with authentic samples by IR and ^{1}H-NMR spectral comparisons.

4-Allyl-2,6-dimethoxy-3-(3-methyl-2-butenyl)phenol (10)——Colorless oil. IR ν_{max} ($CHCl_3$): 3540 (OH), 1638 ($-CH=CH_2$) cm^{-1}. ^{1}H-NMR δ ($CDCl_3$): 6.52 (1H, s), 5.95 (1H, m), 5.52 (1H, br t, $J=6$ Hz), 5.05 (3H, m), 3.86, 3.84 (each 3H, s), 3.31 (4H, br d, $J=6$ Hz), 1.78, 1.69 (each 3H, s). MS *m/e* 262 (M^+), 247, 206, 191, 173, 159, 145, 131, 115, 91.

References and Notes

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13) The structure of **10** was assigned tentatively on the basis of biogenetic considerations, though the possibility exists that the positions of the allyl and prenyl substituents are reversed.