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Phenolic Components from Leaf Oil of *Illicium anisatum* L.

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Four phenolic compounds were isolated from the leaf oil of *Illicium anisatum* L. Spectroscopic and synthetic studies showed that they were 1-allyl-2-methoxy-4,5-methylenedioxybenzene(I), 4-allyl-2,6-dimethoxyphenol(II), 1-allyl-3-methoxy-4-(3-methylbut-2-enyloxy)benzene (III) and 1-allyl-3,5-dimethoxy-4-(3-methylbut-2-enyloxy)benzene (IV). Of the four, III and IV were new compounds.

Keywords——structure determination; leaf oil; phenolic compounds; *Illicium anisatum* L.; chemical synthesis

Investigations on the components of leaf oil of *Illicium anisatum* L. (Japanese name, "Shikimi") (Magnoliaceae) were initiated by J.F. Eijkman,[2] who isolated safrol, eugenol and anethol. No other record of chemical investigations on constituents from the leaves of this plant has been found in the literature. This paper reports the isolations and characterizations of four phenolic compounds 1-allyl-2-methoxy-4,5-methylenedioxy-benzene (I), 4-allyl-2,6-dimethoxyphenol (II), 1-allyl-3-methoxy-4-(3-methylbut-2-enyloxy)benzene (III), and 1-allyl-3,5-dimethoxy-4-(3-methylbut-2-enyloxy)benzene (IV), the latter two being new compounds.

A concentrated methanol extract of the dried leaves of this plant was reextracted with *n*-hexane. Fractionation of the hexane extract on a silica gel column afforded four oily compounds I—IV.

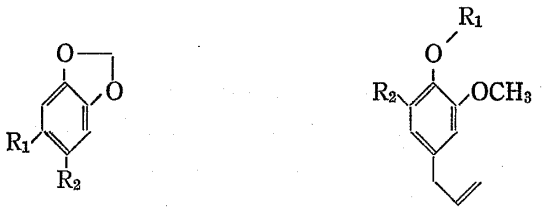
The nuclear magnetic resonance (NMR) spectrum of compound I showed signals at δ 6.62 and δ 6.50 due to two aromatic protons, a methylenedioxy at δ 5.80, a methoxy at δ 3.76 and an allyl group. On the basis of these NMR signals and the parent ion peak in the mass spectrum it seemed likely that compound I was 1-allyl-2-methoxy-4,5-methylenedioxy-benzene, and this structure was confirmed by direct comparison of compound I with an authentic sample synthesized from sesamol (V) by the method of Alexander.[3]

The NMR spectrum of compound II indicated the presence of two methoxy groups (δ 3.76), an allyl group, two aromatic protons (δ 6.36) and an exchangeable proton. The compound was identified as 4-allyl-2,6-dimethoxyphenol (II) by direct comparison with an authentic sample obtained by the usual procedure[4] from 2,6-dimethoxyphenol. There are reports of the isolations of I[5,6] and II[7] from several natural sources but this is the first time they have been found in the leaf oil of *Illicium anisatum* L.

1) Location: *Shomachi, Tokushima, Japan.*
2) J.F. Eijkman, *Ber*, **18**, Ref. 281 (1885); J.F. Eijkman, *Zit. nach C. Wehmer. Die Pflanzenstoffe*, s. 214 (1911).
3) B.H. Alexander, S.I. Gertler, R.T. Brown, T.A. Oda, and M. Beroza, *J. Org. Chem.*, **24**, 1504 (1959).
4) C.J. Coscia, W.J. Schubert, and F.F. Nord, *J. Org. Chem.*, **26**, 5085 (1961).
5) Y. Saiki, T. Saito, H. Sasaki, and S. Fukushima, *Yakugaku Zasshi*, **87**, 1524 (1967); J. Kumamoto and R.W. Scora, *J. Agr. Food. Chem.*, **18**, 544 (1970).
6) The infrared (IR) spectrum of I was identical with that of an authentic sample[5] kindly supplied by Prof. Y. Saiki.
7) A.T. Shulgin, and H.O. Kerlinger, *Naturwiss.*, **51**, 360 (1964); A.O. Lustre and P. Issenberg, *J. Agr. Food. Chem.*, **17**, 1387 (1967).

The molecular weight of III was found to be 232 from the parent ion peak in the mass spectrum. The NMR spectrum of III was very similar to that of eugenol (VI) except for methyl signals at δ 1.76 and δ 1.70, a methylene signal at δ 3.25 and a vinylic proton signal at δ 5.48. These mass and NMR spectral data suggest that III possesses a 3-methylbut-2-enoxy group in place of the hydroxy group in eugenol (VI). Consequently, compound III was identified as 1-allyl-3-methoxy-4-(3-methylbut-2-enyloxy)benzene (*O*-(3-methylbut-2-enyl)-eugenol) by direct comparison with the sample synthesized from eugenol (VI) and 3,3-dimethylallyl chloride.

The NMR spectra of III and IV closely resemble each other except that only the latter has a signal at δ 3.76 (3H, singlet), and that the latter has two aromatic protons at δ 6.30 as a singlet, whereas the former has three aromatic protons, as shown in the experimental part. These findings and the parent peak of compound IV in the mass spectrum at *m/e* 262 suggest that compound IV is 1-allyl-3,5-dimethoxy-4-(3-methylbut-2-enyloxy)benzene. This compound was identified with the sample prepared by reaction of II with 3,3-dimethylallyl chloride.



I: R_1=OCH_3, R_2=CH_2–CH=CH_2
V: R_1=OH, R_2=H

II: R_1=H, R_2=OCH_3
III: R_1=CH_2–CH=C(CH_3)(CH_3), R_2=H
IV: R_1=CH_2–CH=C(CH_3)(CH_3), R_2=OCH_3
VI: R_1,R_2=H

Chart 1

Experimental

Following equipments were used: IR spectra, JASCO DS-701G spectrometer; NMR spectra, JEOL PS-100 spectrometer with tetramethylsilane as an internal reference; mass spectra, JEOL JMS-01SG; Gas liquid chromatography (GLC), Shimadzu gas chromatograph Model GC-6A (10% SE-30 glass column (1.5 m × 0.3 cm), N_2-gas, 50 ml/min, gradient temperature (160—230°, 10°/min)). Thin-layer chromatography (TLC) values were obtained with Kiesel gel G nach Stahl (Merck) as adsorbent. For column chromatography, Merck silica gel with 70—230 mesh and Mallinckrodt silicic acid with 100 mesh were used.

Isolation of I, II, III, and IV——The dried leaves (2.0 kg) of *Illicium anisatum* L. collected in Tokushima prefecture of Japan in Oct. 1974, were extracted with 50 l of methanol at room temperature for 10 days. The methanol solution was concentrated to one-fiftieth of its original volume under reduced pressure at 50°. The resulting oil was treated with *n*-hexane and was divided into soluble and insoluble fractions.

The *n*-hexane soluble fraction was evaporated to give 18.0 g of brown oil. This oil was chromatographed on the column of silica gel (500 g) with chloroform, giving four crude oily substances which have the *Rf* values of 0.8, 0.7, 0.4, and 0.3 on TLC developed with benzene: chloroform (3: 7). Each substances upon rechromatography on silica gel with *n*-hexane: benzene: methylene chloride (4: 3: 3) gave 4.30, 0.22, 8.60 and 0.09 g of colorless oils.

Compound I——Colorless oil (*Rf* 0.8). GLC: one peak with retention time 4.0 min. MS *m/e*: 192 (M^+), 177, 165, 161, 147, 135, 131, 119 *etc.* IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1640 (–CH=CH_2), 2850 (–OMe), 2780 (–OCH_2O–). NMR (δ) $CDCl_3$: 6.62 (1H, s), 6.50 (1H, s), 5.80 (2H, s), 5.70—6.10 (1H, m), 5.00 (2H, m), 3.76 (3H, s), 3.25 (2H, d, J=6 Hz). This compound was identical with an authentic sample synthesized according to the Alexander method[3] (IR spectrum, NMR spectrum and TLC).

Compound II——Colorless oil (*Rf* 0.7). GLC: one peak with retention time 6.5 min. MS *m/e*: 194 (M^+), 179, 177, 163, 161, 151, 147, 133, 119 *etc.* IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH), 1640 (–CH=CH_2), 2850 (–OMe). NMR (δ) $CDCl_3$: 6.36 (2H, s), 5.70—6.10 (1H, m), 5.00 (2H, m), 5.30 (1H, s, D-exchangeable), 3.76 (6H, s), 3.25 (2H, d, J=6 Hz). This compound was identical with an authentic sample prepared by the usual method[4] (IR spectrum, NMR spectrum, and TLC).

Compound III——Colorless oil (*Rf* 0.4). GLC: one peak with retention time 6.8 min. MS *m/e*: 232 (M^+), 164, 149, 133, 121, 104 *etc.* IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1640 (–CH=CH_2), 1675 (R–CH=CR′R″). NMR (δ) $CDCl_3$: 6.58—6.82 (2H, AB type, J=4 Hz), 6.64 (1H, s), 5.70—6.10 (1H, m), 5.48 (1H, t, J=6 Hz), 5.00 (2H, m), 4.44 (2H, d, J=6 Hz), 3.76 (3H, s), 3.25 (2H, d, J=6 Hz), 1.76, 1.70 (each 3H, s).

Compound IV——Colorless oil (*Rf* 0.3). GLC: one peak with retention time 8.0 min. MS *m/e*: 262 (M^+), 246, 221, 194, 179, 153, 151, 147, 133, 131, 119 *etc.* IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1640 (–CH=CH_2), 2850 (–OMe), 1675 (R–CH=CR′R″). NMR (δ) $CDCl_3$: 6.30 (2H, s), 5.70—6.10 (1H, m), 5.48 (1H, t, J=6 Hz), 5.00 (2H, m), 4.36 (2H, d, J=6 Hz), 3.76 (6H, s), 3.25 (2H, d, J=6 Hz), 1.74, 1.66 (each 3H, s).

Synthesis of 1-Allyl-3-methoxy-4-(3-methylbut-2-enyloxy)benzene (III) from Eugenol (VI)——A mixture of 500 mg of eugenol, 750 mg of *t*-BuOK and 500 mg of dimethylallyl chloride was stirred overnight at room temperature. Approximately 100 ml of water was added to the reaction mixture, and the solution was extracted with CH_2Cl_2. The extract was washed with water, dried, and evaporated. The resulting oily residue was chromatographed on silica gel to give 590 mg (83%) of colorless oil. This product was identical with the natural compound (III) (IR spectrum, NMR spectrum, and TLC).

Synthesis of 1-Allyl-3,5-dimethoxy-4-(3-methylbut-2-enyloxy)benzene (IV) from 4-Allyl-2,6-dimethoxyphenol (II)——A solution of 200 mg of II and 340 mg of *t*-BuOK in 2 ml of *t*-BuOH was added 210 mg of 3,3-dimethylallyl chloride with stirring at room temperature. The solution was stirred overnight. After working up in the usual manner, the product was chromatographed on silica gel to give 220 mg (81%) of colorless oil. The product was identical with the natural compound (IV) (IR spectrum, NMR spectrum, and TLC).