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Studies on the Agalwood (Jinkō). IV.[1] Structures of 2-(2-Phenylethyl)chromone Derivatives, Agarotetrol and Isoagarotetrol

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The structures of two compounds, AH_1 and AH_2, isolated from agalwood "Jinkō" were studied. AH_1 was obtained as needles having a melting point different from that of agarotetrol (powder) isolated and characterized by Yoshii *et al.* However, the carbon-13 nuclear magnetic resonance (^{13}C-NMR) data and $[\alpha]_D$ values of the two compounds were identical, and AH_1 was concluded to have the same structure, including stereochemistry, as agarotetrol. The half-chair conformation of the hexenyl ring moiety assumed by Yoshii *et al.* was confirmed by detailed analyses of the proton nuclear magnetic resonance (^{1}H-NMR) and 2D-COSY spectra.

AH_2 was assigned the structure (5*S*,6*R*,7*R*,8*S*)-2-(2-phenylethyl)-5e′,6e,7e,8e′-tetrahydroxy-5,6,7,8-tetrahydrochromone, a stereo-isomer of agarotetrol (7*S*,8*R*), on the basis of the ^{1}H-NMR, X-ray analysis and circular dichroism (CD) spectral data. It was named isoagarotetrol. The hexenyl ring moiety of isoagarotetrol was found to have a half-chair conformation identical to that of agarotetrol in the crystalline state as well as in solution.

Keywords——2-(2-phenylethyl)chromone; agalwood; Aquilariaceae; agarotetrol; isoagarotetrol; ^{1}H-NMR; 2D-COSY; CD; X-ray analysis

Six compounds tentatively named AH_1, AH_2, AH_3, AH_4, AH_5, and AH_6 were previously isolated from agalwood "Jinkō",[1] and the latter four (AH_3—AH_6) were characterized as 6-hydroxy-, 6-methoxy- and 6,7-dimethoxy-2-(2-phenylethyl)chromone and 6-methoxy-2-[2-(3-methoxyphenyl)ethyl]chromone, respectively. This paper deals with structural studies of AH_1 and AH_2.

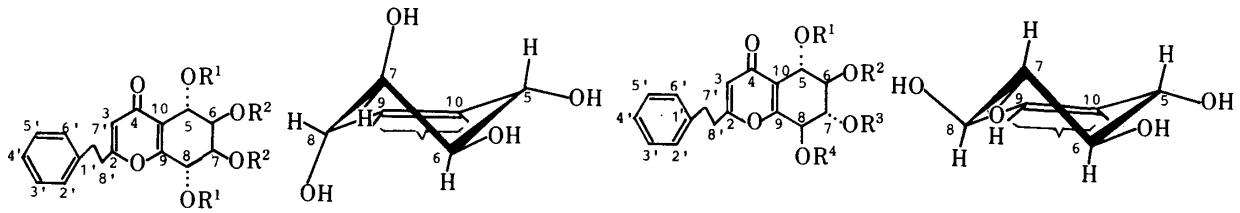
AH_1, colorless needles, $C_{17}H_{18}O_6$, mp 179—181 °C, $[\alpha]_D$ −21.3 °,[2] exhibited absorptions due to a phenylethyl group and a trisubstituted γ-pyrone ring in the infrared (IR) and ultraviolet (UV) spectra, suggesting it to be a compound closely related to agarotetrol (**1**), which had been isolated from agalwood and characterized by Yoshii *et al.*[2] Although AH_1 showed a much higher melting point than that (mp 118—121 °C) reported for **1** (powder, $[\alpha]_D$ −21.9 °), the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectral data (in CD_3OD) as well as the specific rotation were quite similar to those of **1** (Table III). Therefore AH_1 and **1** were considered to have the same structure, including the stereochemistry. Conformational analysis of AH_1 and its derivatives was carried out, particularly to confirm the half-chair conformation of the cyclohexenyl ring and the absolute configuration proposed by Yoshii *et al.* They suggested the cyclohexenyl moiety of **1** to have a pseudoequatorial (e′)5-OH group in contrast to its 5-O acetate, in which the 5-OH group is pseudoaxial (a′), and the difference was thought to be due to the intramolecular hydrogen bonding and the steric and electrostatic repulsions between the pyrone carbonyl and the 5-OAc function.

The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of AH_1 in DMSO-d_6

solution at 24 °C showed four methine protons at δ 3.74, 3.84, 4.32, and 4.48 together with four hydroxy protons at δ 4.96, 5.09, 5.18, and 5.81 which were displaced at 50 °C to δ 4.81, 4.91, 5.03, and 5.68, respectively. The signal at δ 5.81 could be ascribed to the hydroxy proton at C_5 because of the low field displacement due to the intramolecular hydrogen bonding with 4-C=O, and the methine proton at δ 4.32 was assigned as 5-H based on the result of irradiation at δ 5.81. The other methine protons were assigned on the basis of the signal of 5-H by the 2D-COSY and double-irradiation methods as shown in Table I. Therefore the conformation of the hexenyl ring is concluded to be half-chair, having 5e′, 6e, 7a, 8a′-tetrahydroxy groups as assumed by Yoshii *et al.*[2]

In order to determine the absolute configuration of AH_1, its 5,8-diacetoxy-6,7-*p*-methoxybenzoate (**2**) was prepared according to the procedure of Yoshii *et al.*[2] The ^{1}H-NMR spectrum of **2** in C_2D_5OD solution showed the signals of four protons of methines bearing an OCOR group at δ 4.35 (dd), 5.51 (dd), 5.93 (d), and 6.42 (d). In order to corroborate the assignments of 5- and 8-H, **2** was subjected to ^{1}H- and ^{13}C-selective decoupling experiments. On ^{1}H-selective irradiation at δ 5.93, the C_4 signal at δ 178.4 was transformed from a broad singlet ($W_{h/2}$ = *ca.* 4.6 Hz) into a singlet ($W_{h/2}$ = *ca.* 2.3 Hz) and the signal intensity was enhanced by 45%, while irradiation at δ 6.42 did not cause any change of the C_4 signal. Therefore, the proton signal at δ 5.93 is ascribable to 5-H and other protons of **2** were assigned as shown in Table II.

Accordingly, the conformation of the hexenyl ring of **2** is half-chair, bearing 5a′,8e′-diacetoxy-6a,7e-di-*p*-methoxy benzoyl groups. The circular dichroism (CD) spectrum of **2** in ethanol showed a negative chirality of the 6,7-dibenzoate groups. Thus, the absolute configuration of agarotetrol proposed by Yoshii *et al.* was unequivocally confirmed.



1: $R^1=R^2=H$ (agarotetrol)
2: $R^1=CH_3CO$, $R^2=CH_3OC_6H_4CO$

3: $R^1=R^2=R^3=R^4=H$ (isoagarotetrol)
4: $R^1=R^4=H$, $R^2,R^3=>C<^{CH_3}_{CH_3}$
5: $R^1=R^4=CH_3CO$, $R^2,R^3=>C<^{CH_3}_{CH_3}$
6: $R^1=R^4=CH_3CO$, $R^2=R^3=H$
7: $R^1=R^4=CH_3CO$, $R^2=R^3=CH_3OC_6H_4CO$

Chart 1

AH_2 (**3**), colorless plates, $C_{17}H_{18}O_6$, mp 174—175 °C (dec.), $[\alpha]_D$ −58.6° exhibited quite similar absorptions to those of **1** in the IR and UV spectra, suggesting that **3** has a structure related to that of **1**. In the ^{1}H-NMR spectrum of **3** in pyridine-d_5, a broad singlet at δ 8.05 ($W_{h/2}$ = *ca.* 16 Hz) is ascribable to the hydrogen-bonded proton of 5-OH, as in the case of **1**, and three other hydroxy protons appeared at δ 4.99, 6.58, and 7.47 as broad signals ($W_{h/2}$ > 70 Hz) as shown in Table II. Irradiation at δ 8.05 caused the broad doublet at δ 5.13 (5-H) to collapse to a double doublet (J = 6.5, 1.5 Hz). The coupling constant, J = 1.5 Hz, can be interpreted as a homoallylic coupling between 5-H and 8-H. On simultaneous irradiation of two protons at δ 5.42 (8-H, double doublet, J = 6.5, 1.5 Hz) and 8.05, the two double doublets at δ 4.51 (7-H) and 5.13 (5-H) were transformed into two doublets with J = 10.0 and 6.5 Hz, respectively. When a half-chair conformation is assumed for the hexenyl ring moiety,

TABLE I. ^{1}H-NMR Data for AH_1 and AH_2 (**3**) in DMSO-d_6[a)]

	AH_1 Multiplicity (J, Hz)	**3** Multiplicity (J, Hz)
3-H	6.08 s	6.17 s
5-H	4.32 dd (5a′,6a=7.5; 5a′,5-OH=6.0)	4.32 ddd (5a′,6a=7.0; 5a′,5-OH=7.0; 5a′,8a′=1.5)
6-H	3.84 ddd (6a,5a′=7.5; 6a,6-OH=5.5; 6a,7e=2.0)	3.43 dddd (6a,5a′=7.0; 6a,7a=4.5; 6a,6-OH=4.5; 6a,7-OH=4.5)
7-H	3.74 ddd (7e,8e′=4.0; 7e,7-OH=4.0; 7e,6a=2.0)	3.48 dddd (7a,8a′=7.0; 7a,6a=4.5; 7a,7-OH=4.5; 7a,6-OH=4.5)
8-H	4.48 t (8e′,7e=4.0; 8e′,8-OH=4.0)	4.47 ddd (8a′,7a=7.0; 8a′,8-OH=3.0; 8a′,5a′=1.5)
5-OH	5.81 d (5-OH,5a′=6.0)	5.83 dd (5-OH,5a′=7.0; 1.0)
6-OH	5.09 d (6-OH,6a=5.5)	5.22 dd (6-OH,6a=4.5; 1.5)
7-OH	4.96 d (7-OH,7e=4.0)	5.33 dd (7-OH,7a=4.5; 2.0)
8-OH	5.18 d (8-OH,8e′=4.0)	5.13 dd (8-OH,8a′=3.0; 1.5)
7′-H	2.97 m	2.97 m
8′-H	2.87 m	2.89 m
C_6H_5	7.28 m	7.29 m

a) Spectra measured at 400 MHz.

TABLE II. ^{1}H-NMR Data for AH_1, AH_2 (**3**) and Their Derivatives[a)]

	AH_1 (C_5D_5N)	**2** (C_2D_5OD)	**3** (C_5D_5N)	**4** ($CDCl_3$)	**5** ($CDCl_3$)	**6** (C_5D_5N)	**7** ($CDCl_3$)
3-H	6.30 s	6.42 s	6.34 s	6.14 s	6.02 s	6.22 s	6.15 s
5-H	5.52 d, J=7.0	5.93 d, J=3.5	5.13 br d, J=6.5	4.72 d, J=7.2	6.13 d, J=6.0	6.49 d, J=6.7	6.10 d, J=7.2
6-H	5.19 dd, J=7.0, 2.0	4.35 dd, J=3.5, 2.2	4.46 dd, J=10.0, 6.5	3.70 dd, J=8.3, 7.2	3.83 dd, J=7.2, 6.0	4.42 dd, J=8.3, 6.7	5.67 dd, J=8.3, 7.2
7-H	5.05 dd, J=4.0, 2.0	5.51 dd, J=9.0, 2.2	4.51 dd, J=10.0, 6.5	3.82 dd, J=8.3, 6.0	3.96 dd, J=7.2, 6.2	4.49 dd, J=8.3, 6.0	5.71 dd, J=8.3, 6.8
8-H	5.83 d, J=4.0	6.42 d, J=9.0	5.42 dd, J=6.5, 1.5	4.95 d, J=6.0	6.32 d, J=6.2	6.74 d, J=6.0	6.33 d, J=6.8
7′,8′-H	2.82, 2.68 m	2.93 m	2.92, 2.78 m	2.94 m	2.84 m	2.81 m	2.91 m
C_6H_5	7.21 m	7.22 m	7.25 m	7.23 m	7.25 m	7.25 m	7.23 m
$(CH_3)_2C<$				1.50, 1.50 s	1.49, 1.49 s		
CH_3CO		2.07, 2.12 s			2.10, 2.21 s	2.00, 2.20 s	1.86, 1.94 s
CH_3O		3.85, 3.85 s					3.84, 3.84 s
C_6H_4CO		6.94, 6.98, 7.96, 8.01 each d, J=8.0					6.86, 6.87, 7.93, 7.96 each d, J=9.0
5-OH	8.14 br s		8.05 br s				
6-OH	7.30 br s		6.58 br s				
7-OH	7.30 br s		4.99 br s				
8-OH	7.30 br s		7.47 br s				

a) Spectra of AH_1, **2** and **3** measured at 400 MHz, and those of **4**, **5**, **6**, and **7**, at 80 MHz.

the vicinal methine protons should be in a *trans* diaxial relationship, and hence the four hydroxy groups at C_5, C_6, C_7 and C_8 are regarded as being pseudoequatorial (e′), equatorial (e), e and e′, respectively.

However, **3** afforded a monoacetonide (**4**) on standing in an acetone solution with 2,2-dimethoxypropane and *p*-toluenesulfonic acid at room temperature, and its 6,7-isopropylidenedioxy structure was proved by comparison of the ^{1}H-NMR spectra of **3** and **4** (Table II).

TABLE III. ^{13}C-NMR Data for Agarotetrol (**1**), AH_1, AH_2 (**3**), and Their Derivatives

Carbon	**1** (CD_3OD)[2]	AH_1 (CD_3OD)[a]	**2** (C_2D_5OD)	**3** (C_5D_5N)[a]	**4** (C_5D_5N)	**5** (C_5D_5N)	**6** (C_5D_5N)	**7** ($CDCl_3$)
2	171.2	171.2	170.3	169.1	169.4	167.8	167.7	168.6
3	114.0	114.1	114.7[d]	113.6	113.4	113.1	114.1	114.3[e]
4	181.8	182.0	178.4	180.9	181.1	176.9	177.2	176.7
5	70.1	70.1	67.5[b]	71.9	70.5[b]	70.4[b]	72.0[b]	68.1[b]
6	72.5	72.5	69.6[c]	74.8	79.2[c]	75.9[c]	72.5[c]	69.8[c]
7	73.9	73.9	70.6[c]	75.2	79.6[c]	78.2[c]	73.8[c]	70.3[c]
8	66.8	66.8	64.9[b]	70.9	69.0[b]	67.2[b]	70.3[b]	66.6[b]
9	165.1	165.2	160.8	162.5	163.1	159.1	158.9	158.5
10	121.7	121.8	119.9	121.6	122.2	121.3	120.4	120.0
1′	141.1	141.2	140.3	140.4	140.2	140.2	140.4	140.2
2′,6′	129.5	129.6	129.3	128.9	128.9	129.0	129.0	129.0
3′,5′	129.3	129.4	129.0	128.7	128.6	128.6	128.7	128.7
4′	127.3	126.4	127.3	126.8	126.8	126.9	126.8	126.9
7′	33.7	33.7	33.3	32.8	32.6	32.3	32.4	32.5
8′	36.2	36.2	35.7	35.2	34.5	34.7	34.9	34.9
$(CH_3)_2C<$	**5**: 27.2, 27.2, 119.0			**6**: 27.0, 27.0, 114.1				
CH_3COO	**3**: 20.6, 20.6, 170.7, 170.7			**6**: 20.5, 20.8, 169.8, 170.0				
	7: 20.7, 21.1, 170.3, 170.5			**8**: 20.3, 20.6, 169.8, 169.8				
$CH_3OC_6H_4COO$	**3**: 56.0, 56.0, 114.8,[d] 121.8, 121.8, 132.6, 132.6, 165.3, 165.3, 165.5, 165.9							
	8: 55.5, 55.5, 114.3,[e] 121.6, 121.9, 132.4, 164.3, 164.4, 165.1, 165.3							

a) Assignments of 5-, 6-, 7-, and 8-C were established by the selective proton irradiation method. *b*—*e*) May be interchanged in each column.

Therefore, it is also possible that the hexenyl ring of **3** may have a boat conformation in which the four methine protons at C_5, C_6, C_7 and C_8 are all axial, that is, the hydroxy groups at C_6 and C_7 are *cis*-oriented.

In order to determine the configuration of the hexenyl ring moiety of **3**, a single crystal of the 5,8-diacetate of **3** (**6**), $C_{21}H_{22}O_8$, prepared from the diacetate of **4** (**5**), was subjected to X-ray analysis. The crystal data were as follows: size *ca.* $0.05 \times 0.1 \times 0.5$ mm; monoclinic space group $P2_1$ ($Z=2$); cell dimensions $a=21.155$ (20), $b=5.360$ (2), $c=8.810$ (9) Å, $\beta=97.64$, $V=990$ (1) Å^3. In total, 1678 unique intensities were collected by 2θ—ω scan method within $2\theta<120°$ on a Rigaku AFC-5-FOS automated four-circle diffractometer using graphite-monochromated Cu-K_α ($\lambda=1.5418$ Å) radiation.

Twelve plausible atomic positions were revealed by the direct method (MULTAN)[3] and several cycles of isotropic least-squares and subsequent Fourier syntheses gave those of the remaining non-hydrogen atoms. The positions of hydrogen atoms except for those of hydroxy and acetoxy groups were generated computationally on the basis of stereochemical and geometrical considerations. Block-diagonal least-squares refinements with anisotropic thermal parameters for non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms gave a final R value of 0.068 for the total reflections (UNICS III).[4,5]

A perspective drawing of **6** (without solvent atoms) is shown in Fig. 1, and it is evident that the hexenyl ring of **6** has the half-chair and not the boat conformation. The fractional atomic coordinates, bond lengths and bond angles are listed in Tables IV, V and VI, respectively.

The CD spectrum of the di-*p*-methoxybenzoate (**7**) of **6** showed negative chirality.[6] Since the conformations of the hexenyl moieties of **3**, **6** and **7** can be regarded as almost the same based on a comparison of the ^{1}H-NMR spectra, the drawing shown in Fig. 1 represents the absolute structure of **6**.

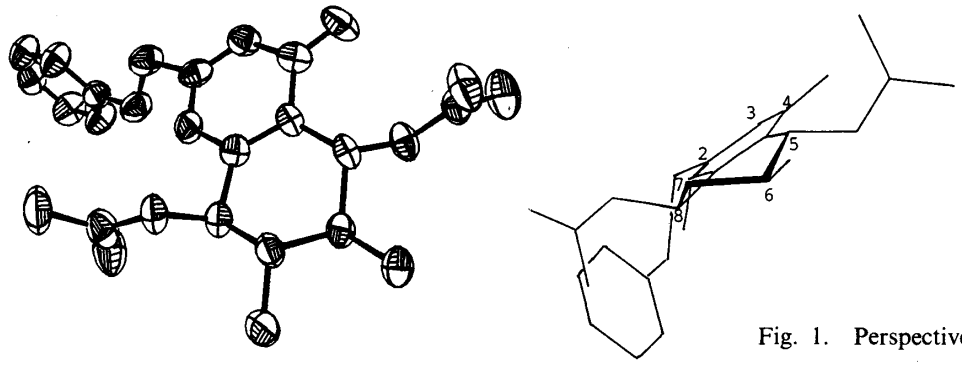


Fig. 1. Perspective Drawing of **6**

TABLE IV. Fractional Atomic Coordinates ($\times 10^4$) and Anisotropic Thermal Parameters ($\times 10^3$)

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C2	1894 (2)	2952 (11)	−877 (6)	36 (3)	47 (3)	68 (2)	−9 (2)	10 (2)	−5 (3)
C3	2135 (2)	1540 (12)	317 (6)	45 (3)	54 (4)	64 (3)	−4 (3)	11 (2)	5 (3)
C4	2793 (2)	1694 (11)	975 (6)	48 (3)	45 (3)	55 (3)	2 (3)	18 (2)	2 (3)
C5	3844 (2)	4101 (11)	928 (5)	41 (2)	45 (3)	28 (2)	8 (3)	2 (2)	8 (3)
C6	4058 (2)	6663 (10)	474 (5)	27 (2)	42 (3)	41 (2)	6 (2)	1 (2)	0 (2)
C7	3908 (2)	6979 (11)	−1274 (5)	38 (2)	46 (3)	36 (2)	1 (2)	0 (2)	8 (2)
C8	3198 (2)	6909 (11)	−1738 (5)	35 (2)	53 (3)	33 (2)	1 (2)	2 (2)	−1 (2)
C9	2883 (2)	4916 (10)	−902 (5)	34 (2)	47 (3)	43 (3)	2 (2)	7 (2)	−1 (2)
C10	3159 (2)	3642 (10)	328 (5)	40 (2)	44 (3)	33 (2)	6 (2)	5 (2)	5 (2)
C1′	231 (2)	5638 (12)	−2342 (6)	48 (3)	58 (4)	57 (3)	−7 (3)	4 (2)	6 (3)
C2′	−43 (3)	3962 (15)	−3453 (7)	54 (3)	76 (5)	73 (4)	−1 (4)	−4 (3)	−15 (4)
C3′	−683 (3)	4186 (16)	−4017 (7)	55 (3)	88 (5)	77 (4)	−4 (4)	−8 (3)	−13 (4)
C4′	−1046 (3)	6050 (15)	−3557 (7)	46 (3)	93 (5)	73 (2)	−1 (4)	−1 (3)	8 (4)
C5′	−782 (3)	7685 (15)	−2460 (8)	48 (3)	85 (5)	95 (5)	4 (3)	9 (3)	−7 (4)
C6′	−147 (3)	7488 (14)	−1887 (7)	51 (3)	73 (5)	79 (4)	−4 (3)	4 (3)	−18 (4)
C7′	932 (2)	5495 (12)	−1706 (7)	45 (3)	58 (4)	75 (4)	−6 (3)	−4 (3)	−3 (3)
C8′	1234 (2)	2946 (12)	−1691 (7)	40 (3)	58 (4)	81 (4)	−9 (3)	4 (3)	0 (3)
C5″	4284 (2)	2451 (11)	3346 (5)	46 (3)	53 (3)	36 (3)	2 (3)	−4 (3)	4 (3)
C5‴	4226 (3)	2536 (15)	5046 (6)	88 (4)	106 (6)	28 (3)	8 (4)	1 (3)	4 (3)
C8″	2597 (2)	7381 (12)	−4227 (6)	41 (3)	68 (4)	51 (3)	5 (3)	2 (2)	14 (3)
C8‴	2493 (3)	6200 (16)	−5783 (6)	72 (4)	104 (6)	36 (3)	−9 (4)	−9 (2)	6 (3)
O2	2266 (1)	4614 (8)	−1509 (4)	32 (2)	59 (2)	49 (2)	−3 (2)	−2 (1)	5 (2)
O4	3028 (2)	260 (8)	1990 (4)	62 (2)	62 (2)	69 (2)	6 (2)	13 (2)	31 (2)
O5	3899 (1)	4152 (8)	2585 (3)	54 (2)	57 (2)	29 (2)	11 (2)	3 (1)	2 (2)
O5′	4636 (2)	1104 (8)	2760 (4)	65 (2)	68 (3)	47 (2)	25 (2)	−5 (2)	3 (2)
O6	4724 (1)	6945 (8)	905 (4)	32 (2)	54 (2)	51 (2)	5 (2)	−3 (2)	3 (2)
O7	4118 (1)	9358 (9)	−1724 (4)	44 (2)	67 (2)	57 (2)	−13 (2)	5 (1)	23 (2)
O8	3083 (1)	6247 (7)	−3349 (3)	40 (2)	63 (2)	33 (2)	4 (2)	−1 (1)	4 (2)
O8′	2290 (2)	9008 (11)	−3781 (5)	79 (3)	100 (4)	67 (2)	35 (3)	−16 (2)	9 (3)

The anisotropic thermal parameters are expressed in the form: $\exp[-2\pi^2(U_{11}h^2a^{*2}+\cdots+2U_{23}klb^*c^*)]$. The standard deviation for the last digit is given in parentheses.

Consequently, **3** is defined as (5*S*,6*R*,7*R*,8*S*)-2-(2-phenylethyl)-5e′,6e,7e,8e′-tetrahydroxy-5,6,7,8-tetrahydrochromone. It is isomeric at C_7 and C_8 to agarotetrol, **1** and we have named it isoagarotetrol.

The 5,6,7,8-tetrahydrochromones bearing a phenylethyl group at C_2, such as **1** and **3** are specific major components so far detected only in the agalwood "Jinkō." They may be of use as reference compounds for identification and possibly for evalution of the quality of agalwoods.

TABLE V. Bond Lengths and Their Standard Deviations (Å)

C2–C3	1.338 (9)	C2–C8′	1.486 (9)	C2–O2	1.359 (7)
C3–C4	1.440 (9)	C4–C10	1.460 (8)	C4–O4	1.233 (8)
C5–C6	1.515 (8)	C5–C10	1.494 (8)	C5–O5	1.451 (7)
C6–C7	1.545 (8)	C6–O6	1.419 (7)	C7–C8	1.504 (9)
C7–O7	1.424 (8)	C8–C9	1.504 (8)	C8–O8	1.452 (7)
C9–C10	1.343 (8)	C9–O2	1.352 (7)	C1′–C2′	1.401 (10)
C1′–C6′	1.369 (10)	C1′–C7′	1.518 (9)	C2′–C3′	1.387 (12)
C3′–C4′	1.357 (12)	C4′–C5′	1.372 (12)	C5′–C6′	1.376 (11)
C7′–C8′	1.515 (9)	C5″–C5‴	1.519 (10)	C5″–O5	1.343 (7)
C5″–O5′	1.202 (8)	C8″–C8‴	1.504 (11)	C8″–O8	1.346 (8)
C8″–O8′	1.185 (9)				

The standard deviation for the last digit is given in parentheses.

TABLE VI. Bond Angles and Their Standard Deviations (°)

C3–C2–O8′	127.8 (6)	C3–C2–O2	121.0 (6)
O8′–C2–O2	111.2 (5)	C2–C3–C4	121.9 (6)
C3–C4–C10	114.9 (5)	C3–C4–O4	123.1 (6)
C6–C5–C10	111.3 (5)	C6–C5–O5	105.0 (5)
C10–C5–O5	107.6 (5)	C5–C6–C7	109.4 (5)
C5–C6–O6	110.3 (5)	C7–C6–O6	108.5 (5)
C6–C7–C8	109.2 (5)	C6–C7–O7	110.0 (5)
C8–C7–O7	106.4 (5)	C7–C8–C9	112.0 (5)
C7–C8–O8	107.4 (5)	C9–C8–O8	106.0 (5)
O8–C9–C10	125.5 (5)	C8–C9–O2	110.9 (5)
C10–C9–O2	123.5 (5)	C4–C10–C5	121.3 (5)
C4–C10–C5	121.3 (5)	C4–C10–C9	118.6 (5)
C5–C10–C9	118.6 (5)	C5–C10–C9	119.9 (5)
C2′–C1′–C6′	118.4 (7)	C2′–C1′–C7′	121.2 (6)
C6′–C1′–C7′	120.3 (6)	C1′–C2′–C3′	118.9 (7)
C2′–C3′–C4′	121.7 (8)	C3′–C4′–C5′	119.5 (8)
C4′–C5′–C6′	119.6 (8)	C1′–C6′–C5′	121.8 (7)
C1′–C7′–C8′	115.9 (6)	C2–C8′–C7′	111.6 (5)
C5‴–C5″–O5	110.5 (5)	C5‴–C5″–O5′	125.4 (6)
O5–C5″–O5′	124.1 (6)	C8‴–C8″–O8′	126.5 (8)
O8–C8″–O8′	123.5 (6)	C2–O2–C9	119.7 (5)
C5–O5–C5″	117.0 (5)	C8–O8–C8″	117.8 (5)

The standard deviation for the last digit is given in parentheses.

Experimental

Melting points were determined on a micro melting point apparatus (Yanagimoto) and are uncorrected. The UV and CD spectra were obtained in EtOH (or MeOH) with a Shimadzu UV-200s spectrometer and a JASCO J-500c spectropolarimeter, respectively, and IR spectra (in KBr disks) with a Shimadzu IR 27G spectrometer. The ^{1}H-NMR spectra were taken on a varian CFT-20 spectrometer at 79.54 MHz and a JEOL JNM GX-400 spectrometer at 399.65 MHz at 24 °C, and ^{13}C-NMR spectra on the Varian CFT-20 at 20.0 MHz and the JEOL JNM GX-400 at 100.4 MHz. Chemical shifts are given in δ (ppm) with tetramethylsilane as an internal standard (s, singlet; d, doublet; t, triplet; dd, double doublet; ddd, double double doublet; dddd, double double double doublet; m, multiplet; br, broad). Column chromatography was performed on Kieselgel 60 (70—230 mesh, Merck).

AH$_1$ (1)——Colorless needles (from MeOH), mp 179—181 °C, $[\alpha]_D^{24}$ −21.3 ° (c=1.02, MeOH). UV λ_{max}^{EtOH} nm (ε): 253 (12000), 208 (15800). IR (KBr). cm^{-1}: 1658, 1600, 1581, 1244, 1182, 1039, 963, 693. *Anal.* Calcd for $C_{17}H_{18}O_6 \cdot 1/2\,H_2O$: C, 62.38; H, 5.85. Found: C, 62.71; H, 6.07. ^{1}H-NMR in DMSO-d_6 and ^{13}C-NMR in CD_3OD: Tables I and III.

Preparation of 5,8-Diacetoxy-6,7-di-*p*-methoxybenzoate (2) of 1——Monoacetonide of **1**: 2,2-Dimethoxypropane (10 ml) and *p*-toluenesulfonic acid (100 mg) were added to **1** (250 mg) suspended in acetone (30 ml), and the mixture

was allowed to stand at room temperature for about 2 h. Then the solution was neutralized with 10% Na_2CO_3, and filtered. The filtrate was evaporated to dryness under reduced pressure and $CHCl_3$ was added to the residue. Insoluble material was removed, and the $CHCl_3$ solution was followed by evaporation to dryness to afford the residue (257.5 mg), which was purified by column chromatography (hexane–AcOEt, 1 : 2, v/v). The major product was recrystallized from ether to give colorless needles (172.9 mg), mp 122—123 °C (dec.), $[\alpha]_D^{30}$ +18.0° (c=1.0, MeOH). IR (KBr) cm^{-1}: 1662, 1601, 1590. UV λ_{max}^{EtOH} nm (ε): 250 (12100), 208 (17100). ^{1}H-NMR (pyridine-d_5): 1.32, 1.36 (each 3H, s, *gem* CH_3), 2.75 (4H, m, CH_2CH_2), 4.76 (1H, br s), 5.11 (2H, br s), 5.83 (1H, br s), 6.29 (1H, s, 3-H), 7.22 (5H, m, aromatic H). *Anal.* Calcd for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19. Found: C, 67.27; H, 6.28. Acetylaltion of Monoacetonide of **1**: An Ac_2O–pyridine (1 : 1, v/v, 5 ml) solution of **1** monoacetonide (50.5 mg) was left to stand overnight and evaporated to dryness under reduced pressure. The residue was purified by column chromatography (hexane–AcOEt, 1 : 1, v/v) and recrystallized from hexane–AcOEt to give colorless plates (38.7 mg), mp 170—171 °C, $[\alpha]_D^{27}$ −9.9° (c=0.9, MeOH). IR (KBr) cm^{-1}: 1760, 1743, 1678, 1632, 1601. UV λ_{max}^{EtOH} nm (ε): 251 (10400), 207 (16900). ^{1}H-NMR ($CDCl_3$): 1.28 1.32 (each 3H, s, *gem* CH_3), 2.04, 2.13 (each 3H, s, CH_3COO), 2.91 (4H, m, CH_2CH_2), 4.57 (2H, t, J=1.2 Hz), 5.19 (1H, t, J=1.2 Hz), 5.70 (1H, t, J=1.2 Hz), 6.14 (1H, s, 3-H), 7.23 (5H, m, aromatic H). *Anal.* Calcd for $C_{24}H_{26}O_8$: C, 65.15; H, 5.92. Found: C, 65.34; H, 5.98. Preparation of the 5,8-diacetate of **1**: A 50% AcOH (10 ml) solution of the 5,8-diacetoxy-6,7-monoacetonide (426 mg) of **1**, was heated on a water bath at 60—70 °C for 24 h. After addition of water (10 ml), the aqueous mixture was extracted with two 20 ml portions of $CHCl_3$. The $CHCl_3$ solution was evaporated to dryness under reduced pressure to afford a residue (400 mg). The major product (170 mg) separated from the residue by column chromatography (hexane–AcOEt, 1 : 2, v/v) was recrystallized from hexane–AcOEt to give colorless needles (140 mg), mp 171—172 °C, $[\alpha]_D^{38}$ −25.6° (c=0.82, $CHCl_3$). UV λ_{max}^{MeOH} nm (ε): 250 (12477), 207 (17468). IR (KBr) cm^{-1}: 3520, 3200, 1760, 1750, 1725, 1670, 1627. ^{1}H-NMR (C_5D_5N): 2.00, 2.19 (each 3H, s, CH_3COO), 2.79 (4H, m, CH_2CH_2), 4.75 (1H, dd, J=8.4, 3.1 Hz, 7-H), 4.82 (1H, dd, J=3.9, 3.1 Hz, 6-H), 6.27 (1H, s, 3-H), 6.73 (1H, d, J=3.9 Hz, 5-H), 6.80 (1H, d, J=8.4 Hz, 8-H), 7.23 (5H, m, aromatic H). *Anal.* Calcd for $C_{21}H_{22}O_8$: C, 62.68; H, 5.51. Found: C, 62.67; H, 5.57.

5,8-Diacetoxy-6,7-di-*p*-methoxybenzoate (**2**): *p*-Methoxybenzoyl chloride (0.8 ml) was added dropwise to a pyridine (5 ml) solution of the 5,8-diacetate (50 mg) of **1** under cooling with ice water, and the reaction mixture was permitted to stand overnight in a refrigerator. After addition of excess MeOH the mixture was evaporated to dryness under reduced pressure. The major product was separated from the residue by column chromatography (hexane–AcOEt, 1 : 1, v/v) and further purified by repeated column chromatography with the use of $CHCl_3$ to give a colorless amorphous product. $[\alpha]_D^{28}$ −80.6° (c=1.03, MeOH). UV λ_{max}^{MeOH} (ε): 258 (54924), 210 (56195). CD (c=0.12 × 10^{-4}, methanol) $\Delta\varepsilon^{25}$: +7.6 (254) (positive maximum), −17.5 (271) (negative maximum). IR (KBr) cm^{-1}: 1752, 1720, 1670, 1610. *Anal.* Calcd for $C_{37}H_{34}O_{12} \cdot 1/2\,H_2O$: C, 65.39; H, 5.46. Found: C, 65.67; H, 5.46. ^{1}H- and ^{13}C-NMR: Tables II and III.

AH_2 (3)——Colorless plates (from MeOH), mp 174—175 °C (dec.), $[\alpha]_D^{29}$ −58.6° (c=1.19, MeOH). UV λ_{max}^{EtOH} nm (ε): 252 (13450), 208 (17300). IR (KBr) cm^{-1}: 1660, 1600, 1582, 1250, 1199, 1042, 968, 697. *Anal.* Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 64.13; H, 5.86.

Monoacetonide (4) of 3——2,2-Dimethoxypropane (5 ml) containing *p*-toluenesulfonic acid (100 mg) was added to an acetone (20 ml) solution of **3** (157 mg), and the mixture was allowed to stand at room temperature for 4 h. The solution was neutralized with 10% Na_2CO_3. The resulting precipitates were removed by filtration and the filtrate was evaporated to dryness under reduced pressure. Acetone was added to the residue and insoluble material was filtered off. The filtrate was evaporated again to give a residue (181 mg), which was purified by column chromatography using hexane–AcOEt (1 : 1.5, v/v). The major product (107 mg) was recrystallized from hexane–AcOEt to give colorless needles (88 mg), mp 162—163 °C, $[\alpha]_D^{14}$ −85.0° (c=1.0, MeOH). UV λ_{max}^{EtOH} nm (ε): 252 (9300), 208 (12800). IR (KBr) cm^{-1}: 3450, 3300, 1641, 1581, 1571. *Anal.* Calcd for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19. Found: C, 67.31; H, 6.36. ^{1}H- and ^{13}C-NMR: Tables II and III.

5,8-Diacetate (5) of 4——**4** (185 mg) was dissolved in a mixture of Ac_2O (5 ml) and pyridine (5 ml). The mixture was left standing overnight, and evaporated to dryness under reduced pressure. The residue (206 mg) was chromatographed by using hexane–AcOEt (1 : 1, v/v) to afford colorless needles (190 mg), which were crystallized from hexane–acetone solution, mp 175—178 °C (dec.), $[\alpha]_D^{33}$ +11.67° (c=1.2, MeOH). UV λ_{max}^{EtOH} nm (ε): 250 (11600), 208 (18300). *Anal.* Calcd for $C_{24}H_{26}O_8$: C, 65.15; H, 5.92. Found: C, 64.97; H, 6.15. ^{1}H- and ^{13}C-NMR: Tables II and III.

5,8-Diacetate (6) of 3——**5** (148 mg) was dissolved in 3% trifluoroacetic acid (8 ml), and the solution was heated on a water bath at 60 °C for 1 h. On cooling, the mixture gave a precipitate, which was separated by filtration, and washed with water. The precipitates (105 mg) were refined by column chromatography ($CHCl_3$–MeOH, 15 : 1, v/v) to afford colorless needles (from MeOH) of **6** (60 mg). The filtrate was neutralized with Na_2CO_3 solution and the mixture was evaporated to dryness under reduced pressure. The residue was separated to give two fractions by column chromatography ($CHCl_3$–MeOH, 15 : 1, v/v). The less polar fraction (10 mg) was recrystallized from MeOH to give colorless needles of **6**, mp 189—191 °C, $[\alpha]_D^{22}$ +46.15° (c=1.04, MeOH). UV λ_{max}^{EtOH} nm (ε): 249 (11300), 208 (16700). IR (KBr) cm^{-1}: 3480, 1740, 1725, 1715, 1665, 1630. *Anal.* Calcd for $C_{21}H_{22}O_8$: C, 62.68; H, 5.51. Found: C, 62.81; H, 5.56. The product in another fraction (15 mg) was not examined. ^{1}H- and ^{13}C-NMR: Tables II and III.

Di-*p*-methoxybenzoate (7) of 6——*p*-Methoxybenzoyl chloride (0.5 ml) was added dropwise to a pyridine (3.5 ml) solution of **6** (38 mg) under cooling with ice water, and the reaction mixture was allowed to stand overnight in a refrigerator. After addition of MeOH, the solution was evaporated to dryness under reduced pressure. The residue was purified by column chromatography (hexane–AcOEt, 1 : 1, v/v), and the dried eluate gave **7** (62 mg) as a colorless amorphous product, $[\alpha]_D^{27}$ $-46.3°$ ($c=0.8$, MeOH). UV λ_{max}^{EtOH} nm (ε): 259 (46600), 209 (45000). CD ($c=0.84\times10^{-4}$, EtOH) $\Delta_{\varepsilon}^{25}$: +25.3 (240) (positive maximum), −38.5 (269) (negative maximum). IR (KBr) cm^{-1}: 1750, 1720, 1665, 1630, 1602, 1580. *Anal.* Calcd for $C_{37}H_{34}O_{12}\cdot H_2O$: C, 64.53; H, 5.27. Found: C, 64.80; H, 4.98. ^1H- and ^{13}C-NMR: Tables II and III.

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