Communications to the Editor

[Chem. Pharm. Bull. 34(11)4889—4891(1986)]

THE STRUCTURES OF AH_{10} AND AH_{11}, NOBEL BI-PHENYLETHYLCHROMONES FROM AGALWOOD

Kiyoshi Iwagoe,[a] Tenji Konishi,[a] Shiu Kiyosawa,*,[a] Yasuo Shimada,[b]
Kazumoto Miyahara,[c] and Toshio Kawasaki[c]
Kyoto Pharmaceutical University,[a] Nakauchi-cho, Misasagi, Yamashina-ku, Kyoto, 607, Japan, Mitsuboshi Seiyaku Company,[b] 153, Gose-shi, Nara, 639-22, Japan, and Faucalty of Pharmaceutical Sciences, Setsunan University,[c] 45-1, Nagaotōge-cho, Hirakata, Osaka, 573-01, Japan

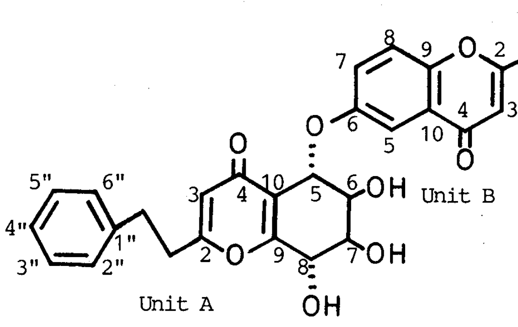
New bi-2-(2-phenylethyl)chromones, tentatively named AH_{10} and AH_{11} were isolated from Agalwood "Jinkō" and their structures were determined.

KEYWORDS——— bi-2-(2-phenylethyl)chromone; agalwood; Aquilariaceae; ^1H-NMR; ^{13}C-NMR

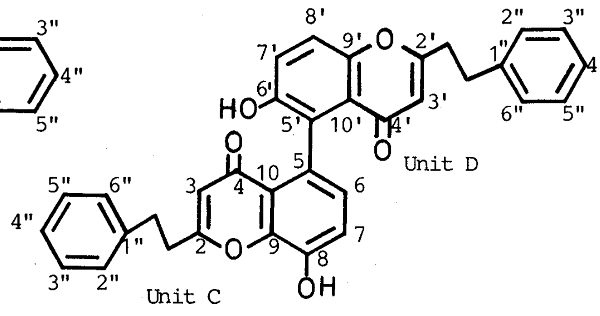
New bi-phenylethylchromones, AH_{10} and AH_{11} were isolated from the acetone extracts of agalwood "Jinkō" from Kalimantan, along with other related compounds.[1)] This paper describes the characterization of these structures.

AH_{10} (1), a white powder (mp 110°C), $[\alpha]_D$ −127.7° (MeOH) showed a molecular ion at m/z 566 in the FD-MS giving the molecular formula $C_{34}H_{30}O_8$. The IR (KBr) and UV (MeOH) spectra of 1 exhibited strong absorption maxima due to a γ-pyrone ring (1662, 1639, 1610, and 1582 cm^{-1}; 241 nm, ε=35818). The ^1H-NMR spectrum (400 MHz, DMSO-d_6) showed the presence of one pair of proton signals at δ 6.16 and 6.22 (each s, 3-H) and two sets of phenylethyl groups, indicating the structure bi-2-(2-phenylethyl)-chromone derivative for 1, considering the molecular weight. One unit of the dimer was considered to be agarotetrol[2)] on the basis of four methine proton signals indicating a hexenyl ring structure of 5/6 trans, 6/7 cis, and 7/8 trans in accordance with the vicinal coupling systems at δ 3.89, 4.27, 4.59, and 5.33 (Table I). The doublet signal of the methine proton at δ 5.33 should be assigned to 5-H because of the downfield position, considered to result from the bonding of the ether at C_5 to another monomeric unit. The assignment of 5-H is supported by the absence of the proton signal of 5-OH which should be found in a field lower than the other three hydroxylic protons at C_6, C_7 and C_8. This is because of the intramolecular bonding with 4-C=O as displayed by ^1H-NMR spectra of agarotetrol and isoagarotetrol.[1b)] Furthermore, the possibility of the hydrogen bond between 4-C=O and 5-OH was not present in the ^{13}C-NMR spectrum, which exhibited chemical shift at the carbon 4-C=O about 2 ppm upfield from that of agarotetrol (Table II).[1b)] The other methine protons were assigned on the basis of the signal of 5-H together with three hydroxyl protons which showed upfield displacement as the temperature increased, as shown in Table I.

NII-Electronic Library Service



1



3

Acetylation (Ac$_2$O-pyridine) of 1 afforded triacetate (2), a white powder (mp 82-83°C), $[\alpha]_D$ -43.6° (MeOH), ^{1}H-NMR (CDCl$_3$, δ):2.02, 2.11, 2.12 (each s, CH$_3$COO), 5.40 (d, J=7.2, 5-H), 5.56 (dd, J=4.1,2.0, 7-H), 5.64 (dd, J=7.2,2.0, 6-H), 6.08 (d, J=4.1, 8-H). Therefore, the acetylation did not convert the half-chair form in the hexenyl ring of 1 from (5S)-5e'-OH to (5S)-5a'-OAc.3) Subsequently, the structure of one monomeric unit (Unit A) was found to be agarotetrol linked at C$_5$ by the ether bond to another monomeric unit (Unit B).

The structure of Unit B was characterized as 6-alkoxy-2-(2-phenylethyl)chromone, based on the appearance of three proton signals of the aromatic ABX system similar to that of AH$_4$,1a) a 6-methoxy derivative of 2-(2-phenylethyl)chromone, in the ^{1}H- and ^{13}C-NMR spectra of 1 (Tables I and II).

Accordingly, the structure of AH$_{10}$ was elucidated as (5S,6S,7R,8S)-2-(2-phenylethyl-6,7,8-trihydroxy-5,6,7,8-tetrahydro-5-[2-(2-phenylethyl)chromonyl-6-oxy]chromone, 1.

AH$_{11}$ (3), a pale yellowish powder (mp 239-242°C) exhibited the absorptions due to the γ-pyrone ring in the IR (KBr):1640, 1600, 1580 cm^{-1} spectrum and the UV λ_{max} (MeOH):234 nm (ε=42977) spectrum. The ^{1}H-NMR spectrum (80 MHz, DMSO-d$_6$) showed that 3 is another dimeric derivative of 2-(2-phenylethyl)chromone on the basis of two singlet signals of 3-H at δ 5.78 and 5.86.

Acetylation (Ac$_2$O-pyridine) of 3 afforded diacetate (4), colorless needles, mp 240°C, FD-MS m/z: M$^+$ 614, ^{1}H-NMR (400 MHz, CDCl$_3$,δ): 1.86, 2.42 (each s, CH$_3$COO), 2.87, 3.01 (each m, CH$_2$CH$_2$), 5.90, 5.93 (each s, 3-H), 7.20, 7.22, and 7.30 (2H, 4H, and 4H, respectively, each m, aromatic H). Two sets of the ortho coupling signals at δ 6.97, 7.36 (each d, J=8.0, 6- and 7-H, Unit C), 7.39 and 7.50 (each d, J=8.8, 7- and 8-H, Unit D), due to the protons of the chromone ring, were assigned by comparing them with those of AH$_3$1a) and AH$_7$1c) bearing 6-hydroxyl and 5,8-dihydroxyl groups, respectively. Therefore, it appeares that compound 3 has a dimeric structure of 2-(2-phenylethyl)chromone linked by a C-C bond at each C$_5$, and two hydroxyl groups should be separately situated in either monomeric unit at the positions of C$_6$ and C$_8$. This structure was consistent with the result of 2D-NOSYN of 4, suggesting the presence of a 6-acetoxyl function (δ 1.85) which exhibited cross peaks with 3-, 6- and 7-H attached to another chromone ring having an 8-acetoxyl group. Further, in the ^{13}C-NMR spectrum of 4 the chemical shifts of C$_5$-C$_{10}$ in each chromone ring showed excellent agreement with the calculated values as shown in Table II.

Accordingly, AH$_{11}$ was determined to be 2,2'-di-(2-phenylethyl)-8,6'-dihydroxy-5,5'-bichromone, 3.

Table I. ^{1}H-NMR data for AH$_{10}$ in DMSO-d_6 (ppm, 25°C)

	Unit A			Unit B
5-H	5.33 (d, J=8.2 Hz)			7.78 (d, J=3.0 Hz)
6-H	4.27 (ddd, J=8.2,6.5,2.0 Hz)			
7-H	3.89 (ddd, J=4.2,3.5,2.0 Hz)			7.62 (dd, J=8.5,3.0 Hz)
8-H	4.59 (dd, J=5.5,3.5 Hz)			7.66 (d, J=8.5 Hz)
6-OH	5.65 (d, J=6.5 Hz)	(5.49)*)		Unit A and B
7-OH	5.35 (d, J=4.2 Hz)	(5.29)	CH_2CH_2	2.61 (m,4H), 3.02 (m,4H)
8-OH	5.51 (d, J=5.5 Hz)	(5.45)	3-H	6.16 (s,1H), 6.22 (s,1H)
			C_6H_5	6.98 (2H), 7.18 (4H), 7.27 (4H)

*) Chemical shifts obtained at 50°C are indicated in parentheses.

Table II. ^{13}C-NMR Data for AH$_{10}$, AH$_{11}$ and AH$_{11}$ Diacetate

	AH$_{10}$ (1)[a]		AH$_{11}$ (3)		AH$_{11}$ Diacetate (4)	
Carbon	Unit A	Unit B	Unit C	Unit D	Unit C	Unit D
2,2'	168.7	168.3	166.5	166.5	166.8	167.6
3,3'	113.8	110.5	109.5	109.8	110.7	111.1
4,4'	179.7	177.5	177.5	177.5	177.4	177.4
5,5'	78.9	109.6	129.2	122.9	134.7 (135.6)[b]	128.9 (131.4)
6,6'	71.0	157.7	127.1	150.3	125.6 (124.6)	145.2 (146.6)
7,7'	74.7	124.9	121.1	117.6	128.3 (127.2)	125.6 (127.2)
8,8'	66.4	119.7	144.9	116.9	139.4 (139.4)	118.6 (117.4)
9,9'	160.7	151.9	151.0	144.9	149.3 (149.2)	155.1 (153.1)
10,10'	123.7	124.7	122.1	126.2	123.3 (123.5)	125.6 (123.5)
1"	140.3	140.5	140.2	140.2	140.5	140.6
2",6"	128.8	128.9	128.4	128.4	128.9	128.9
3",5"	128.5	128.7	128.3	128.3	128.7	128.7
4"	126.6	126.8	126.2	126.2	126.7	126.7
CH_2CH_2	32.6 35.2	32.9 35.7	31.9 34.3	31.9 34.3	32.6 35.4	32.7 35.4
$\underline{C}H_3\underline{C}OO$					20.1, 177.4	20.4, 177.7

a) Assignments were established by comparing with the data for agarotetrol (AH$_1$)[1b] and AH$_4$.[1a]

b) Calculated values[1,4] are indicated in parentheses.

It is worthy of note that the structures of AH$_{10}$ and AH$_{11}$, as the first of biphenylethylchromones were made up in the form of ether or C-C linkage between two 2-(2-phenylethyl)chromones, hydroxylated or hydrogenated.

ACKNOWLEDGEMENTS The authors are grateful to Mr. M. Nishi of Setsunan University for the ^{1}H-NMR and 2D-NOSYN spectra. Thanks are also due to Mr. Fujiwara (^{1}H- and ^{13}C-NMR) and Miss M. Takahashi (FD-MS) of Kyoto Pharmaceutical University.

REFERENCES AND NOTES

1) a) Y. Shimada, T. Tominaga, T. Konishi, and S. Kiyosawa, Chem. Pharm. Bull., 30, 3791 (1982); b) Y. Shimada, T. Konishi, S. Kiyosawa, M. Nishi, K. Miyahara, and T. Kawasaki, Chem. Pharm. Bull., 34, 2766 (1986); c) S. Shimada, T. Konishi, S. Kiyosawa, M. Nishi, K. Miyahara, and T. Kawasaki, The 106th Annual Meeting of the Pharmaceutical Society of Japan, Chiba, April, 1986. ^{1}H-NMR (80 MHz, $CDCl_3$, δ) of 5,8-diacetoxy-2-(2-phenylethyl)chromone (AH$_7$ 5,8-diacetate): 6.95, 7.38 (each d, J=8.6 Hz, 6- and 7-H).

2) ^{1}H-NMR (400 MHz, DMSO-d_6, δ) of agarotetrol (AH$_1$): 3.74 (ddd, J=4.0,4.0,2.0 Hz, 7-H), 3.84 (ddd, J=7.5,5.5,2.0 Hz, 6-H), 4.32 (dd, J=7.5,6.0 Hz, 5-H), 4.48 (t, J=4.0,4.0 Hz, 8-H), 4.96 (d, J=4.0 Hz, 7-OH), 5.09 (d, J=5.5 Hz, 6-OH), 5.18 (d, J=4.0, 8-OH), 5.81 (d, J=6.0 Hz, 5-OH).[1b]

3) E. Yoshii, T. Koizumi, and T. Oribe, Tetrahedron Lett., 41, 3921 (1978).

4) D. F. Ewing, Org. Magn. Reson., 12, 499 (1979).

(Received September 12, 1986)