Studies on the Agalwood (Jinkō). XI. Structure of Dioxan-Linked Bi-phenylethylchromone Derivative

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New dioxan-linked bi-2-(2-phenylethyl)chromone, tentatively named AH₂₁ was isolated from a pyridine extract of agalwood "Jinkō" and structurally characterized using proton and carbon-13 nuclear magnetic resonance spectra.

Keywords bi-2-(2-phenylethyl)chromone; agalwood; Aquilariaceae; dioxan-linkage; ¹H-NMR; ¹³C-NMR; NOE

2-(2-Phenylethyl)chromone derivatives occur in agalwood "Jinkō" in various stages of polymerization. More recently six dimeric and four trimeric derivatives of 2-(2-phenylethyl)chromone have been found in the acetone and pyridine extracts of agalwood.¹⁾ A new bi-2-(2-phenylethyl)chromone, AH₂₁, was isolated from the pyridine extracts of agalwood from Kalimantan.^{1d)}

This paper describes the characterization of the structure.

AH₂₁ (**1**), white powder (mp 123—125 °C), [α]_D -75.2° (MeOH), in the infrared (IR) and ultraviolet (UV) spectra showed absorption maxima due to a γ -pyrone ring; 1660, 1630, 1600 cm⁻¹ and 247 nm, ϵ =25971. It was suggested to be a bi-2-(2-phenylethyl)chromone derivative by its proton nuclear magnetic resonance (¹H-NMR) spectrum, which showed the presence of a pair of singlets at δ 6.07 and 6.13, and two sets of phenylethyl groups. One unit (unit A) of the dimer was considered to be agarotetrol²⁾ on the basis of the vicinal coupling system of four methine protons

at δ 3.88, 4.30, 4.57 and 5.21 on the cyclohexene ring moiety of 5,6,7,8-tetrahydrochromone. Two hydroxy protons at δ 5.33 and 5.49 were confirmed by the saturation transfer method decreasing the signals of OH protons. The methine proton at δ 5.21 merely showed a doublet signal (J =7.9 Hz) coupled between the vicinal methine proton at δ 4.30, and it was ascribed to the C₅ position in comparison with the coupling constants of agarotetrol between 5- and 6-H. The downfield shift was considered to result from the bonding of ether at C₅ to another monomeric unit (unit B). The assignment of 5-H was also supported by the absence of the proton signal of 5-OH, which should appear in a field lower than the other hydroxylic protons at C₆, C₇ and C₈ because of the intramolecular bonding between 5-OH and 4-CO³⁾; further, the carbon signal of 4-CO exhibited a chemical shift about 2 ppm upfield from that of agarotetrol in the carbon-13 nuclear magnetic resonance (¹³C-NMR) spectrum.^{1a)} The double doublet methine proton at δ 4.30 was assigned to 6-H on the basis of the double-irradiation

Fig. 1. ¹H-¹³C Shift Correlated Spectrum AH₂₁ (**1**) in DMSO-*d*₆

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Chart 1

TABLE I. ^1H -NMR Spectral Data for AH_{21} (δ in $\text{DMSO}-d_6$)

Unit A			Unit B		
5-H	5.21	(1H, d, $J=7.9$)	5'-H	7.78	(1H, s)
6-H	4.30	(1H, dd, $J=7.9, 2.0$)			
7-H	3.88	(1H, ddd, $J=4.0, 3.5, 2.0$)			
8-H	4.57	(1H, dd, $J=4.9, 4.0$)	8'-H	6.99	(1H, s)
7-OH	5.33	(1H, d, $J=3.5$)			
8-OH	5.49	(1H, d, $J=4.9$)			
3-H	6.07	(1H, s)	3'-H	6.13	(1H, s)
CH_2CH_2	2.63	(4H, m)	CH_2CH_2	2.97	(4H, m)
C_6H_5	7.00	(2H, dd, $J=8.1, 1.7$), 7.13, 7.78 (each 4H, m)			

TABLE II. ^{13}C -NMR Spectral Data for AH_{21} (δ in $\text{DMSO}-d_6$)

Carbon	Unit A	Carbon	Unit B	Carbon	Unit A	Unit B
2	167.72	2'	167.54	1'', 1'''	139.97	139.74
3	113.01	3'	108.01	2'', 6''	128.21	128.16
4	177.89	4'	175.85	2'', 6'''		
5	78.27	5'	109.99	3'', 5''	127.97	127.97
6	68.70	6'	146.84	3'', 6'''		
7	73.13	7'	153.70	7'', 7'''	31.52	32.01
8	64.14	8'	103.25	8'', 8'''	34.13	34.42
9	159.81	9'	152.39			
10	121.41	10'	115.40			

method between the 5-H signal, which showed the absence of the geminal coupling system with a hydroxy proton; thus the two hydroxy protons at δ 5.33 and 5.49 were ascribed to 7- and 8-OH, respectively. Subsequently, unit A was found to be agarotetrol dioxan-linked at C_5 and C_6 , respectively to another monomeric unit B.

The structure of unit B was assumed to be the 6,7-dialkoxylate of 2-(2-phenylethyl)chromone because of the presence of two singlet signals of the aromatic protons at δ 7.78 and 6.99. The two protons were assigned to locations of C_5' and C_8' by ^1H and ^{13}C shift-correlated spectrum (2D-COSY) (Fig. 1, Tables I and II).⁴⁾ The two ether bonding positions between unit A and B were determined by measuring the difference in nuclear Overhauser effect (NOE) spectrum; irradiation of the 5-H at δ 5.21 caused an appreciable NOE increase of the 5'-H proton signal at δ 7.78 and further showed an NOE increment of the 8'-H at δ 6.99 upon irradiation of the 6-H of unit A at 60°C solution (Fig. 2). Therefore, it was determined that the C_5 and C_6 of unit A were linked via

Fig. 2. NOEs of AH_{21} (1) (%)

an ether bridge to C_6' and C_7' , respectively, in unit B.

Accordingly, AH_{21} was characterized as the dioxan-linked bi-2-(2-phenylethyl)chromone, 1.

The polymers of 2-(2-phenylethyl)chromones isolated so far from "Jinkō" have proved to be dimers and trimers linked by ether bonds at the 5,6'-, 5,7'- or 8,6'-positions between agarotetrol or isoagarotetrol and another 2-(2-phenylethyl)chromone derivative. AH_{21} is specific as the first of a dioxan-linked biphenylethyl chromone derivative formed at the 5,6'- and 6,7'-positions between agarotetrol and 2-(2-phenylethyl)chromone.

Experimental

Isolation of AH_{21} A pyridine extract (300 g) from residue-2⁴⁾ was refluxed with MeOH to obtain a viscous extract (56.5 g) which, as a result of silica gel column chromatography (CHCl_3 -MeOH- H_2O , 90:10:1 v/v), gave four fractions (monitored by thin layer chromatography (TLC) with detection under UV light). Fraction 1 (8.57 g) was chromatographed on silanized silica gel (MeOH- H_2O , 2:3 v/v) followed by silica gel (CHCl_3 -MeOH- H_2O , 100:10:1 v/v) to give two fractions, A (543 mg) and B (1.18 g). Fraction A was subjected to column chromatography on Sephadex LH-20 (MeOH) and a silica gel (AcOEt-MeOH- H_2O , 10:1:0.1 v/v) to give three fractions, fr.₁ (236 mg), fr.₂ (190 mg) and fr.₃ (240 mg). Fr.₂ was followed with preparative high performance liquid chromatography on Lobar Rp-8 (acetonitrile- H_2O , 4:6 v/v) on a recycle preparative gel partition chromatography (column: Jaigel-310, elution: 4.0 ml/min, detection; UV) to afford AH_{21} as a white powder (14 mg) from AcOEt-MeOH.

AH_{21} (1): White powder (mp 123–125°C). $[\alpha]_D^{25} -75.2^\circ$ ($c=1.09$, MeOH). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 232 (28229), 247 (25971), IR (KBr) cm^{-1} : 3370 (OH), 1660, 1630, 1600 (γ -pyrone), 738, 690 (benzene ring). Field desorption mass spectrum (FD-MS) m/z : 565 $[\text{M}+\text{H}]^+$, 547 $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$, 282 $[\text{C}_{17}\text{H}_{14}\text{O}_4]^+$, 192 $[\text{C}_{10}\text{H}_8\text{O}_4]^+$. ^1H -NMR and ^{13}C -NMR: Tables I and II.

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