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The Position of Glucose Linkage in Phillyrin

The position of glucose linkage in phillyrin (**1**) was established to be at C-4″ by the discussion of ^{13}C nuclear magnetic resonance (^{13}C-NMR) spectra of phillygenin methyl ether (**2**), phillygenin (**3**) and phillygenin acetate (**4**).

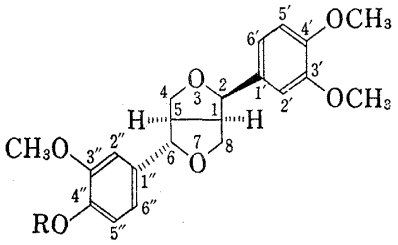
Keywords——^{13}C-NMR; phillyrin; position of glucose linkage; phillygenin methyl ether; phillygenin; phillygenin acetate

In previous papers[1,2] we reported the isolation of phillyrin (**1**), $C_{27}H_{34}O_{11}\cdot 1/2H_2O$, mp 146—148°, $[\alpha]_D^{21}$ +46.9° (c=0.25, MeOH), from fruit of *Forsythia suspensa* VAHL (Oleaceae), which is one of the original plants of "FORSYTHIAE FRUCTUS" listed in the Japanese Pharmacopoeia Ed. IX.

1 is glucoside of (+)-epipinoresinol monomethyl ether isolated first from genus *Phillyrea* by Carboncini.[3]

The position (C-4′ or C-4″) of glucose linkage with aglycone has been undetermined as yet.[4]

In this communication we could establish the position by the discussion of ^{13}C-NMR spectra of aglycone derivatives.



1: R=β-D-glucose
2: R=CH_3
3: R=H
4: R=CH_3CO

Fig. 1

The aglycone was obtained by hydrolysis of **1** with β-glucosidase (Miles Laboratoires Ltd.).

The physical data[5] of derivatives used in this experiment are as follows. Phillygenin methyl ether (**2**), $C_{22}H_{26}O_6$, mp 126—128°, $[\alpha]_D^{25}$ +99° (c=0.10, MeOH), UV λ_{max}^{MeOH} nm (log ε): 231.5 (4.26), 279 (3.79), IR ν_{max}^{KBr} cm^{-1}: 1600, 1590, 1519 (C=C), PMR δ: 6.83—7.10 (6H, m, arom.H), 4.88 (1H, d, J=5 Hz, H-2), 4.48 (1H, d, J=7 Hz, H-6), 3.67—4.33 (4H, m, H-4,8), 3.93 (12H, s, 4×OCH_3), 2.67—3.57 (2H, m, H-1,5); Phillygenin (**3**), $C_{21}H_{24}O_6$, mp 133—134°, $[\alpha]_D^{22}$ +120° (c=0.04, MeOH), UV λ_{max}^{MeOH} nm (log ε): 231.5 (4.25), 280 (3.83), IR ν_{max}^{KBr} cm^{-1}: 3430 (OH), 1600, 1585, 1510 (C=C), PMR δ: 6.87 (6H, br.s, arom.H), 5.43—5.80 (1H, br. OH), 4.87 (1H, d, J=5 Hz, H-2), 4.43 (1H, d, J=7 Hz, H-6), 3.70—4.30 (4H, m, H-4,8), 3.88 (9H, s, 3×OCH_3), 2.73—3.57 (2H, m, H-1,5); Phillygenin acetate (**4**), $C_{23}H_{26}O_7$, mp 122.5—123.0°, $[\alpha]_D^{25}$ +98.3° (c=0.29, MeOH), UV λ_{max}^{MeOH} nm (log ε): 223.5 (4.20), 279.3 (3.77), IR ν_{max}^{KBr} cm^{-1}: 1760 (CO), 1600, 1590, 1518 (C=C), PMR δ: 6.73—7.13 (6H, m, arom.H), 4.85 (1H, d, J=5 Hz, H-2), 4.50 (1H, d, J=7 Hz, H-6), 3.63—4.33 (4H, m, H-4,8), 3.83, 3.87, 3.90 (9H, each s, 3×OCH_3), 2.77—3.53 (2H, m, H-1,5), 2.30 (3H, s, 1×CH_3CO).

^{13}C-NMR spectral data[6] are given in Table I.

Recently Pelter, *et al.*[7] reported that 1′ and 1″ carbon atoms of axial and equatorial aryl

1) S. Nishibe, M. Chiba, and S. Hisada, *Yakugaku Zasshi*, **97**, 1134 (1977).
2) S. Nishibe, M. Chiba, and S. Hisada, *Shoyakugaku Zasshi*, **31**, 131 (1977).
3) Carboncini, *Pharmacie* **8**, 323 (1836).
4) J. Gripenberg, *Acta Chem. Scand.*, **3**, 898 (1949).
5) All the melting points were determined on a Yanagimoto Micro Melting Point apparatus and are not corrected. The following instruments were used: Optical rotation values, Yanagimoto OR-10; Ultraviolet (UV) spectra, Shimadzu UV-210; Infrared (IR) spectra, Shimadzu IR-400; Proton nuclear magnetic resonance (PMR) spectra, Jeol JNM-PMX 60 in $CDCl_3$ solution with tetramethylsilane (TMS) as internal reference.
6) ^{13}C-NMR spectra were recorded on Jeol FX 60 spectrometer, equipped with JEC-980 computer using 8K data points. Each sample was dissolved into $CDCl_3$ in a 10 mm sample tube.
7) A. Pelter, R.S. Ward, E.V. Rao, and K.V. Sastry, *Tetrahedron*, **32**, 2783 (1976).

Table I. ^{13}C-NMR Spectra of Aglycone Derivatives[a]

Carbon	Derivatives		
	2	3	4
1	50.2	50.2	50.2
2	82.1	82.1	82.1
5	54.5	54.5	54.6
6	87.7	87.8	87.4
8	69.8	69.7	69.8
4	71.1	71.1	71.1
1′	131.0	131.0	131.0
1″	133.8	133.1	140.3
2′	109.1	108.6	109.1
2″	109.2	109.1	110.0
3′	148.8	148.9	148.9
3″	149.3	146.8	151.3
4′	148.1	148.1	148.1
4″	148.8	145.4	139.2
5′	111.1	111.2	111.2
5″		114.3	122.7
6′	117.8	117.8	117.8
6″	118.5	119.2	118.1
OCH_3	56.0	55.9	55.9
$\underline{C}H_3CO-$			20.7
$CH_3\underline{C}O-$			169.1

a) All values given as ppm downfield from TMS.

groups of 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane lignans are clearly distinct from each other in ^{13}C-NMR spectra, that is, the signals of former being assigned to be at around 131 ppm, the latter at around 134 ppm for veratryl group.

In comparison of the spectral data between these three derivatives, the appreciable differences of chemical shift values for C-1″ (equatorial aryl group) at 133.8 ppm of **2**, 133.1 ppm of **3** and 140.3 ppm of **4** were observed by aryl carbon shielding due to the effect of substituent at the *para* position, while the differences for C-1′ (axial aryl group) at around 131 ppm were not observed.

These results lead to conclusion that the glucose linkage in **1** is at C-4″ position.

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Faculty of Pharmaceutical Sciences
Higashi Nippon Gakuen University
Ishikari-Tobetsu, Hokkaido,
061-02, Japan

Mariko Chiba
Sueo Hisada
Sansei Nishibe

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