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Effects of *O*-Methylation and *O*-Glucosylation on Carbon-13 Nuclear Magnetic Resonance Chemical Shifts of Matairesinol, (+)-Pinoresinol and (+)-Epipinoresinol

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The effects of *O*-methylation and *O*-glucosylation on the carbon-13 nuclear magnetic resonance chemical shifts of matairesinol (**1**), (+)-pinoresinol (**6**) and (+)-epipinoresinol (**11**) are discussed.

The chemical shifts of carbons on the 2,3-dibenzylated butyrolactone and 2,6-diarylated 3,7-dioxabicyclo[3.3.0]octane rings are not affected by methylation and glucosylation of hydroxy groups on the aromatic rings.

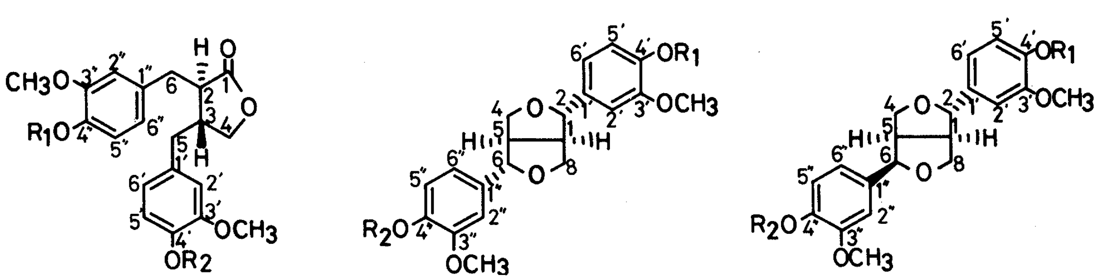
As regards the chemical shifts of aromatic carbons caused by *O*-methylation, all the 1′(1″), 3′(3″), and 4′(4″) carbons of the guaiacyl unit are characteristically shifted downfield by 1.6±0.1, 1.3±0.1, and 2.4±0.1 ppm, respectively, while the 5′(5″) carbons are shifted upfield by 3.5±0.1 ppm. In the case of the chemical shifts of aromatic carbons caused by *O*-glucosylation, all the 1′(1″) and 3′(3″) carbons of the guaiacyl unit are characteristically shifted downfield by 3.0±0.1 and 1.3±0.1 ppm, respectively.

Keywords——^{13}C-NMR; *O*-methylation shift; *O*-glucosylation shift; ligan; matairesinol; (+)-pinoresinol; (+)-epipinoresinol; guaiacyl group

Carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectral studies on the effect of *O*-methylation of *ortho*-substituted phenols on the aryl carbon shielding have been reported.[1,2] In addition, the effects of *O*-glucosylation on the ^{13}C-NMR chemical shifts of coumarins have been reported.[3]

The shift values caused by simple chemical derivations of phenolic compounds are expected to have wide application to the structural elucidation of natural products by means of ^{13}C-NMR spectral analysis.

This paper deals with the effects of *O*-methylation and *O*-glucosylation on the ^{13}C-NMR chemical shifts of lignans, matairesinol (**1**), (+)-pinoresinol (**6**), and (+)-epipinoresinol (**11**).



1: $R_1=R_2=H$
2: $R_1=H,\ R_2=CH_3$
3: $R_1=R_2=CH_3$
4: $R_1=glc,\ R_2=H$
5: $R_1=glc,\ R_2=CH_3$

6: $R_1=R_2=H$
7: $R_1=H,\ R_2=CH_3$
8: $R_1=R_2=CH_3$
9: $R_1=glc,\ R_2=H$
10: $R_1=glc,\ R_2=CH_3$

11: $R_1=R_2=H$
12: $R_1=H,\ R_2=CH_3$
13: $R_1=R_2=CH_3$
14: $R_1=glc,\ R_2=H$
15: $R_1=glc,\ R_2=CH_3$

Chart

Experimental

^{13}C-NMR spectra were measured with a JEOL FX-60 spectrometer operating at 15.00 Mz, equipped with a JEC-980 computer. The spectra of samples were taken in a micro-cell in dimethyl sulfoxide (DMSO)-d_6 with tetramethylsilane (TMS) as an internal standard. Chemical shifts are given on the δ scale (ppm).

Samples——Compounds **1**, **2**, **4**, **5**, **6**, **9**, **12**, and **15** were isolated from *Forsythia* fruits (Oleaceae).[4-6] Compound **14** was isolated from *Symplocos lucida* SIEB. *et* ZUCC. (Symplocaceae).[7] Compounds **3**, **8**, **10**, and **13** were prepared from **1**, **6**, **9**, and **12**, respectively, by methylation with diazomethane.[4-6] Compound **7** was prepared from **10** by hydrolysis with emulsin in the usual way.[8] Compound **11** was prepared from **6** by acid treatment as described below.

(+)-Epipinoresinol (11)——Compound **6** (1 g) was dissolved in glacial acetic acid (6 ml), the solution was cooled and perchloric acid (0.4 ml) was added to it. After 3 d at room temperature, the solution was diluted with water and extracted with chloroform. The extract was washed with sodium hydrogen carbonate solution. The solvent was evaporated to yield a dark gum. This was purified by preparative thin-layer chromatography to give **11** (293.4 mg). $[\alpha]_D^{24}$ +118.4° ($c=0.3$ in $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 232 (4.08), 281.5 (3.64). UV $\lambda_{max}^{EtOH+NaOH}$ nm: 252.5, 295.5. IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1610, 1520 (arom. C=C). MS m/z: 358 (M^+, $C_{20}H_{22}O_6$), ^{1}H-NMR (in $CDCl_3$), δ: 2.73—3.45 (2H, m, $C_{1,5}$–H), 3.50—4.20 (4H, m, $C_{4,8}$–H), 3.90 (6H, s, 2 × OCH_3), 4.37 (1H, d, $J=5$ Hz, C_6–H), 4.82 (1H, d, $J=7$ Hz, C_2–H), 5.53 (2H, s, 2 × OH, quenched by addition of D_2O), 6.60—6.95 (6H, m, arom. H).

These spectral data are in agreement with those described in the literature.[9]

Results and Discussion

The assignment of chemical shifts of the carbon nuclei was carried out mostly on the basis of the signal multiplicity in off-resonance decoupled spectra and the additivity rule of

TABLE I. ^{13}C-NMR Chemical Shifts and *O*-Methylation and *O*-Glucosylation Shifts[a]

	1	**2**	$\Delta\delta$ (**2**−**1**)	**3**	$\Delta\delta$ (**3**−**1**)	**4**	$\Delta\delta$ (**4**−**1**)	**5**	$\Delta\delta$ (**5**−**1**)
C-1	178.4	178.3		178.2		178.4		178.4	
C-2	45.5	45.5		45.5		45.4		45.5	
C-3	43.7	43.7		43.7		43.7		43.7	
C-4	70.6	70.6		70.6		70.6		70.6	
C-5	35.3	35.3		35.3		35.3		35.3	
C-6	33.6	33.6		33.6		33.5		33.5	
C-1′	129.5	131.2	+1.7	131.1	+1.6	129.5		131.2	+1.7
C-1″	128.8	128.8		130.5	+1.7	131.8	+3.0	131.8	+3.0
C-2′	112.7	112.4		112.4		112.7		112.5	
C-2″	113.4	113.4		113.1		113.8		113.9	
C-3′	147.4	148.6	+1.2	148.6	+1.2	147.4		148.7	+1.3
C-3″	147.4	147.3		148.5	+1.1	148.6	+1.2	148.7	+1.3
C-4′	144.9	147.3	+2.4	147.3	+2.4	144.9		147.4	+2.5
C-4″	145.0	145.0		147.4	+2.4	145.2		145.3	
C-5′	115.3	111.9	−3.4	111.8	−3.5	115.3		111.9	−3.4
C-5″	115.3	115.2		111.7	−3.6	115.1		115.2	
C-6′	120.7	120.3		120.3		120.7		120.5	
C-6″	121.5	121.5		121.2		121.2		121.3	
OCH_3	55.4	55.3		55.4		55.5		55.4	
		55.4				55.6		55.7	
Glc-1						100.2		100.3	
Glc-2						73.2		73.2	
Glc-3						76.8		76.9	
Glc-4						69.6		69.7	
Glc-5						76.8		76.9	
Glc-6						60.6		60.7	

[a] Significant shift values above 0.5 ppm are shown.

TABLE II. ^{13}C-NMR Chemical Shifts and *O*-Methylation and *O*-Glucosylation Shifts[a)]

	6	**7**	$\Delta\delta$ (**7**−**6**)	**8**	$\Delta\delta$ (**8**−**6**)	**9**	$\Delta\delta$ (**9**−**6**)	**10**	$\Delta\delta$ (**10**−**6**)
C-1	53.6	53.6		53.7		53.5		53.5	
C-5									
C-4	70.9	70.8		71.0		71.0		71.0	
C-8									
C-2	85.2	85.1		85.0		84.8		84.8	
C-6		84.9				85.1			
C-1′	132.3	132.2		134.0	+1.7	135.3	+3.0	135.1	+2.8
C-1″	132.3	133.9	+1.6	134.0	+1.7	132.2		133.8	+1.5
C-2′	110.5	110.5		110.0		110.5		110.5	
C-2″	110.5	110.0		110.0		110.5		109.9	
C-3′	147.6	147.4		148.9	+1.3	149.0	+1.4	148.9	+1.3
C-3″	147.6	148.8	+1.2	148.9	+1.3	147.5		148.7	+1.1
C-4′	145.9	145.9		148.3	+2.4	145.9		145.8	
C-4″	145.9	148.1	+2.2	148.3	+2.4	145.9		148.1	+2.2
C-5′	115.2	115.1		111.7	−3.5	115.1		115.2	
C-5″	115.2	111.7	−3.5	111.7	−3.5	115.1		111.6	−3.6
C-6′	118.6	118.5		118.1		118.1		118.1	
C-6″	118.6	118.1		118.1		118.6		118.1	
OCH_3	55.6	55.4		55.4		55.6		55.4	
								55.6	
Glc-1						100.3		100.1	
Glc-2						73.2		73.1	
Glc-3						76.9		76.8	
Glc-4						69.7		69.6	
Glc-5						76.9		76.8	
Glc-6						60.7		60.6	

a) Significant shift values above 0.5 ppm are shown.

substituent effects.[10)] The assignments of the carbon pairs, 3′ and 4′ carbons or 3″ and 4″ carbons in **1**, **6**, and **11**, were confirmed by examination of proton-coupled spectra.[1,11)]

The chemical shift values and chemical shift differences for methylates and glucosides, calculated with respect to the signal positions for the parent lignans, **1**, **6**, and **11**, are summarized in Tables I, II, and III.

The chemical shifts of the 1, 2, 3, 4, 5, and 6 carbons of the 2,3-dibenzylated butyrolactone ring of **1** are not affected by methylation and glucosylation of hydroxy groups on the aromatic rings. The chemical shifts of the 1,5, 2,6, and 4,8-carbons of the 2,6-diarylated 3,7-dioxabicyclo[3.3.0]octane ring of **6** and **11** are sensitive to the stereochemistry but not to *O*-methylation and *O*-glucosylation on the aromatic rings. The chemical shifts of the 1′ and 1″ carbons of the guaiacyl unit in 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane lignans are markedly sensitive to the stereochemistry. The chemical shift values are 132.3 ppm for an equatorial guaiacyl unit and 129.6 ppm for an axial guaiacyl unit. On the other hand, the chemical shifts of the 2′,2″, 3′,3″, 4′,4″, 5′,5″, and 6′,6″ carbons are not very sensitive to the stereochemistry.

As regards the chemical shifts of aromatic carbons caused by *O*-methylation, all the 1′(1″) 3′(3″) and 4′(4″) carbons of the guaiacyl unit are characteristically shifted downfield by 1.6±0.1, 1.3±0.1 and 2.4±0.1 ppm, respectively, while the 5′(5″) carbons are shifted upfield by 3.5±0.1 ppm. In the case of the chemical shifts of aromatic carbons caused by *O*-glucosylation, all the 1′(1″) and 3′(3″) carbons of the guaiacyl unit are characteristically

TABLE III. ^{13}C-NMR Chemical Shifts and *O*-Methylation and *O*-Glucosylation Shifts[a]

	11	**12**	$\Delta\delta$ (**12**−**11**)	**13**	$\Delta\delta$ (**13**−**11**)	**14**	$\Delta\delta$ (**14**−**11**)	**15**	$\Delta\delta$ (**15**−**11**)
C-1	53.7	53.9		53.9		54.0		54.0	
C-5	49.3	49.4		49.3		49.4		49.4	
C-4	68.7	68.9		68.8		69.0		69.0	
C-8	70.2	70.4		70.3		70.4		70.4	
C-2	86.9	87.1		86.7		86.7		86.8	
C-6	81.3	81.3		81.2		81.4		81.3	
C-1′	132.3	132.4		134.0	+1.7	135.4	+3.1	135.4	+3.1
C-1″	129.6	131.3	+1.7	131.2	+1.6	129.6		131.2	+1.6
C-2′	110.3	110.3		109.9		110.4		110.5	
C-2″	109.8	109.5		109.5		109.9		109.5	
C-3′	147.4	147.6		148.8	+1.4	149.0	+1.6	149.0	+1.6
C-3″	147.2	148.5	+1.3	148.5	+1.3	147.3		148.5	+1.3
C-4′	145.9	146.0		148.3	+2.4	145.9		146.0	
C-4″	145.2	147.6	+2.4	147.6	+2.4	145.3		147.7	+2.5
C-5′	115.1	115.1		111.6	−3.5	115.2		115.1	
C-5″	115.1	111.6	−3.5	111.6	−3.5	115.3		111.6	−3.5
C-6′	118.5	118.7		118.2		118.3		118.3	
C-6″	117.8	117.7		117.5		117.9		117.7	
OCH_3	55.5	55.5		55.4		55.7		55.6	
Glc-1						100.2		100.3	
Glc-2						73.3		73.2	
Glc-3						76.8		76.9	
Glc-4						69.8		69.8	
Glc-5						77.0		76.9	
Glc-6						60.8		60.8	

a) Significant shift values above 0.5 ppm are shown.

shifted downfield by 3.0 ± 0.1 and 1.3 ± 0.1 ppm, respectively. Therefore we would suggest that the careful measurement of chemical shift differences between methylates or glucosides and parent lignans may provide valuable information for structural elucidation, since lignans which have an *ortho*-substituted phenol group in their structure occur commonly in nature.

The application of these results to the structural elucidation of new lignans from *Olea* bark will be reported in separate papers.[12,13]

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