

PARAMAGNETIC INDUCED SHIFTS IN THE NMR SPECTRA OF FLAVONE COMPOUNDS BY  $\text{Eu}(\text{FOD})_3$

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In the work of structure elucidation of naturally occurring biflavones we have occasionally encountered a problem to determine the position of linkage between two flavone nuclei. For example, natural hinokiflavone (8, R=H) had been considered to have another structure (9, R=H) before a synthetic proof was given.<sup>1</sup> The method of NMR solvent induced shifts was reported to be useful for resolution of the problem.<sup>2</sup> However, it must be used with the greatest caution in such a case as saharanflavone heptamethyl ether<sup>3</sup> because of an unusual shift value of the aromatic methoxy group. We now report on the studies of paramagnetic induced shifts of flavone compounds due to addition of  $\text{Eu}(\text{FOD})_3$ , suggesting a method to distinguish a proton attached to either C-6 or C-8 of flavone nucleus because H-6 showed much larger shift values than H-8.

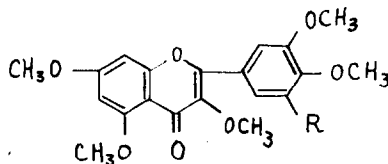
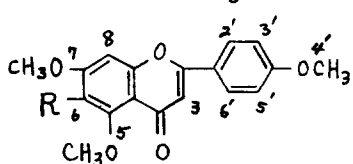
Four compounds (No. 1 ~ 4) examined preliminarily are listed in Table 1, in which the magnitude of the induced change in the chemical shift of every proton is represented by "S-value" proposed by A. F. Cockerill and D. M. Rackham<sup>4</sup> as the slope of straight line<sup>5</sup> obtained by plotting the shift value against the molar ratio of  $\text{Eu}(\text{FOD})_3$  to a flavone compound. The results obtained are summarized as follows: a)  $\text{OCH}_3$ -5 showed the largest shifts (12.34 ~ 18.88 ppm) meaning that complexations occur mostly at neighbouring carbonyl group, b) H-6 showed considerable shifts (5.70 ~ 7.16 ppm) when compared with those of H-8 (1.12 ~ 1.56 ppm), c) H or  $\text{OCH}_3$  attached to side phenyl groups showed the least shifts, and d) H-3 (-1.54, 0.08 ppm) and  $\text{OCH}_3$ -3 (0.80, 0.92 ppm) showed rather small shifts in comparison with  $\text{OCH}_3$ -6 (5.16 ppm) and  $\text{OCH}_3$ -7 (1.02 ~ 1.28 ppm) whose position is at a distance from carbonyl group. It is noteworthy that the H-3 of

Table 1. S-Values<sup>‡</sup> of Flavone Compounds by Eu(FOD)<sub>3</sub>

Positions	Compounds			
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
3	0.08	-1.54	(0.80)	(0.92)*
5	(13.34)	(12.34)	(14.08)	(18.88)
6	6.32	(5.16)	5.70	7.16
7	(1.12)	(1.02)	(1.28)	(1.14)*
8	1.56	1.18	1.12	1.30
2',6'	0	-0.50	0.46	0.46
3',5'	-0.02	-0.26	0.14, (0.12)	(0.12)
4'	(0)	(-0.18)	(0.04)	(0.32)

1. apigenin trimethyl ether, 2. 6-hydroxyapigenin tetramethyl ether, 3. quercetin pentamethyl ether, 4. myricetin hexamethyl ether.

‡ See the text. \* Assignment is tentative. Parentheses show methoxy proton shifts. Spectra were taken on a JEOL PS-100 instrument using TMS as internal standard in a CDCl<sub>3</sub> solution.

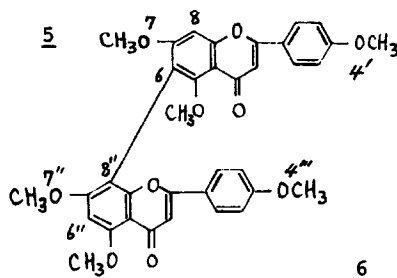
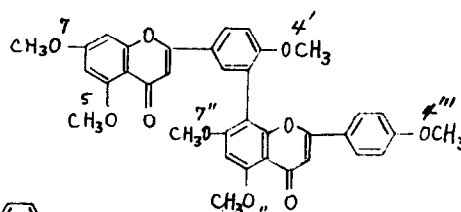
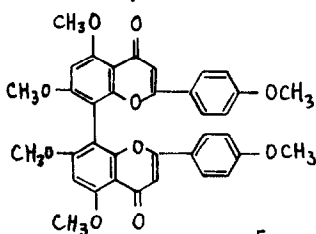


1. R=H

3. R=H

2. R=OCH<sub>3</sub>

4. R=OCH<sub>3</sub>

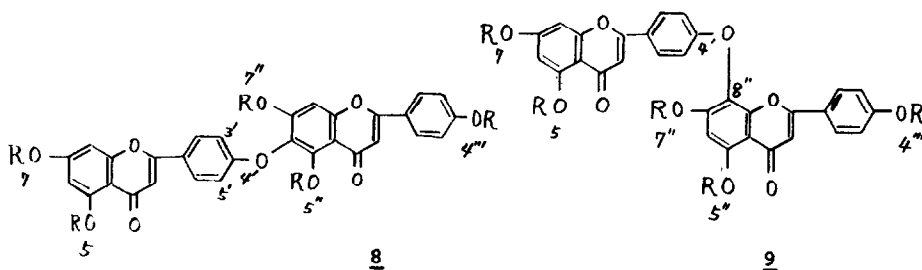


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Table 2. S-Values<sup>#</sup> of Fully Methylated Biflavones by Eu(FOD)<sub>3</sub>

Protons	Compounds				
	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>
OCH <sub>3</sub> -5	7.34	2.14	6.12	10.02	{ 6.88
5"		11.16	8.78	4.38	{ 6.60
7	0.72	0.44	0.36	0.80	{ 0.82
7"		2.04	1.06	0.58	{ 0.52
4'	-0.06	{ 0.02	{ 0.12	--	--
4"		{ -0.08	{ -0.08	-0.06	-0.10
H -3	0.18	0.28	0.02	-0.06	0.14
3"		0.06	-0.16	0.36*	0.26
6	3.66	--	2.76	4.80	3.36
6"		5.80	4.24	--	3.52
8	--	0.64	0.50	1.14	0.72
8"		--	--	0.74*	--
2', 6'	0.56	0.08	-0.36, 0	0.04	-0.02
2'', 6''		0.52	-0.12	-0.14	0
3', 5'	0.24	0.02	-- , 0.10	2.00	-0.10
3'', 5''		0.06	-0.08	-0.08	0.18

5. hexa-O-methylcupressuflavone,      6. hexa-O-methylagathisflavone,  
7. hexa-O-methylamentoflavone,      8. penta-O-methylhinokiflavone,  
9. penta-O-methyl 4'-8'' biapigenyl ether. Other notes are given in Table 1.



compound 2 showed an upfield shift<sup>6</sup> (-1.54 ppm) because of a larger  $\theta$  value in the McConnell-Robertson equation,  $S=K(3 \cos^2\theta - 1)/r^3$  for the pseudocontact shift.<sup>7</sup>

Five compounds (No. 5 ~ 9) listed in Table 2 are all fully methylated biflavones and on addition of Eu(FOD)<sub>3</sub> they showed the same tendency of shifts

as the four compounds given in Table 1. In these compounds, a half amount of used reagent is effective to each flavone nucleus when the same molar ratio of reagent was added. However, OCH<sub>3</sub>-5 and 5" showed different shift values from each other except a symmetrical compound, No. 5. This fact means that the complexation of Eu(FOD)<sub>3</sub> to both flavone nuclei is not even but characteristic to each compound due to their chemical structures. It is interesting that H-3' and 5' of compound No. 8 showed a much larger shift value (2.00 ppm) than those (-0.10 ~ 0.24 ppm) of the other compounds perhaps because the side phenyl group is attached to 6-position of the other flavone nucleus.

The largest shift value among those of H-8 and 8" is 1.14 ppm (No. 8), which is still much smaller value than those of H-6 and 6" (2.76 ~ 5.80 ppm). This fact will make it possible to distinguish a proton attached to either C-6 or C-8, accordingly to elucidate the structure of biflavones which have a flavone - flavone linkage at C-6 or C-8.

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