

ANALYSIS OF THE PMR SPECTRA OF 3- AND
5-SUBSTITUTED FLAVONES WITH PARAMAGNETIC
ADDITIVES

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On the basis of an analysis of the PMR spectra of flavons and its 3- and 5-hydroxy and methoxy derivatives by means of the method of paramagnetic additives, it is assumed that there are different relative orientations of the A, B, and C rings in flavone and its derivatives.

In the present paper we report the results of an analysis of the PMR spectra of flavone and its 3- and 5-hydroxy and methoxy derivatives. The literature contains fragmentary data on this problem without presentation of the complete interpretation of the spectra [1, 2].

The protons of the A, B, and C rings of the flavone molecule resonate over a relatively narrow range (6.5-8.2 ppm), and this hinders the unambiguous interpretation of the spectra. There is no doubt about the assignment of the signals of the protons of the methoxy and hydroxy groups and of the singlet of the 3-H proton at 6.5-6.9 ppm.

When the double-resonance method was used, the two doublets in the spectrum of 5-methoxyflavone at δ 6.71 and 6.98 ppm were assigned to the 6-H and 8-H protons, with $\delta_8 > \delta_6$. The doublets of the 6-H and 8-H protons in the spectrum of 5-hydroxyflavone were similarly assigned.

In order to obtain a more complete interpretation of the PMR spectra discussed in the present paper, we used the method of paramagnetic additives with tris(dipivaloylmethanato)europium [Eu(DPM)₃], inasmuch as this compound can induce greater paramagnetic pseudocontact shifts without substantial broadening of the resonance lines [3]. On the basis of data on the basicities of flavones [4], we suppose that these compounds should be coordinated with Eu(DPM)₃ at the acyclic oxygen atom.

The spectrum of 3-methoxyflavone with (B) and without (A) the Eu(DPM)₃ additive is presented in Fig. 1. The concentration of the ligand was more than 10 times higher than the concentration of the complexing salt. Inasmuch as the paramagnetic shifts are inversely proportional to the cube of the distance (r) from the coordinating ion to the resonating nuclei, it follows from an analysis of the structure of 3-methoxyflavone in Stuart models with allowance for the angular factor ($3 \cos^2 \theta - 1$) [5] in our case that the signals of the 5-H and CH₃O protons should experience the greatest shift. We therefore assigned the doublet at weak field (Fig. 1, spectrum B) to the 5-H proton. Consequently, this proton in the PMR spectrum of 3-methoxyflavone without the additive also resonates at weakest field causing the appearance of a doublet of quartets, just as in the spectrum of flavone, because of spin-spin coupling with 6-, 7-, and 8-H. The signal of the 5-H proton, which is closest to the site of coordination, experiences the greatest broadening when Eu(DPM)₃ is added to the sample. Its splitting therefore does not appear in the spectrum in Fig. 1B because of spin-spin coupling with 7- and 8-H.

When a sample of 3-methoxyflavone containing the paramagnetic additive was exposed to an additional radio-frequency field corresponding to the signal of the 5-H proton, we assigned the multiplet

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TABLE 1. Parameters of the PMR Spectra of Flavones

Compound	δ , ppm*								J, Hz
	3-H	5-H	6-H	8-H	2'-H	6'-H	OCH ₃	OH	
Flavone	6,81s	8,23dq			8,00m				J_{56} 7,5; J_{78} 7,5; J_{57} 1,8; J_{68} 2,0; J_{58} 0,8
3-Hydroxyflavone		8,19†			8,19†			7,01s	
3-Methoxyflavone		8,24dq			8,05m		3,94s		J_{56} 7,5; J_{57} 1,7; J_{58} 0,7
5-Hydroxyflavone	6,76s		6,73dd	6,88dd	7,89m			12,39s	J_{67} 8,5; J_{78} 1,8; J_{68} 1,0
5-Methoxyflavone	6,49s		6,71dd	6,98dd	7,80m		3,90s		J_{67} 8,0; J_{78} 8,0; J_{68} 1,0

* The following abbreviations were used: s is singlet, d is doublet, dd is doublet of doublets, dq is doublet of quartets, and m is multiplet.

† The 5-H, 2'-H, and 6'-H signals overlap and form an unseparable multiplet.

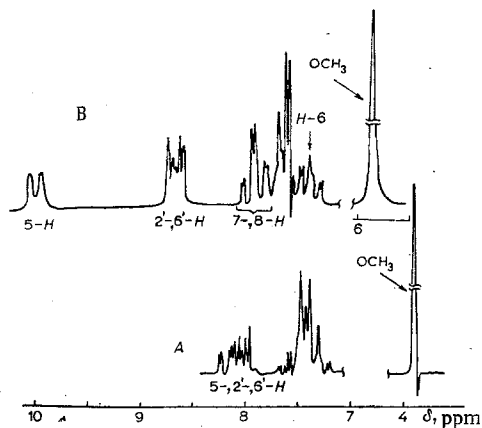


Fig. 1. PMR spectrum of 3-methoxyflavones at room temperature with (A) and without (B) the $\text{Eu}(\text{DPM})_3$ additive.

centered at δ 8.63 ppm, which is twice as intense as the doublet at weak field, to the 2'- and 6'-H protons. Using the double-resonance method, one can also assign the signals of the remaining protons in the PMR spectrum of 3-methoxyflavone containing the $\text{Eu}(\text{DPM})_3$ additive. Thus the triplet is due to the 6-H proton, and 3'-, 4'-, 5'-, 7-, and 8-H resonate further to the weakfield side (Fig. 1, spectrum B).

The use of the method of paramagnetic additives led to good results in the interpretation of the spectra of flavone and 5-methoxyflavone and made it possible to determine the spin-spin coupling constants (Table 1). Unfortunately, we were unable to thoroughly analyze the PMR spectra of 3- and 5-flavones in this manner, inasmuch as when $\text{Eu}(\text{DPM})_3$ was added to the samples of these compounds, the expected shift of the signals was not observed in their PMR spectra, although the resonance lines broadened markedly. Inasmuch as the broadenings observed in the spectra because of hyperfine interaction and shift of the resonance lines depend on the temperature [5], we re-

corded the PMR spectra of 3-hydroxyflavone at various temperatures. However, an increase in the temperature does not improve the form of the signals, and the spectrum, just as at room temperature, remains virtually uninformative. One's attention is directed to the fact that the signal of the protons of the tert-butyl groups of $\text{Eu}(\text{DPM})_3$ is not shifted to strong field with respect to hexamethyldisiloxane when it is added to solutions of 3- and 5-hydroxyflavones but appears at weaker field. Thus the PMR spectra of 3- and 5-hydroxyflavones do not undergo changes characteristic for paramagnetic complexes with exchanged ligands, inasmuch as $\text{Eu}(\text{DPM})_3$ probably forms stable diamagnetic complexes with these compounds. On the basis of the results of the above-presented experiments and with allowance for the integral intensities, we assumed that the 5-, 2'-, and 6'-H protons, the signals of which overlap and give a poorly resolved multiplet, resonate at weakest field in the PMR spectrum of 3-hydroxyflavone.

It seemed of interest to compare the PMR spectra of the flavones by comparing the paramagnetic shifts (δ') induced by $\text{Eu}(\text{DPM})_3$. Comparable δ' values were taken from the spectra recorded in the presence of approximately identical excesses of the ligands, inasmuch as it did not seem possible to construct the concentration dependences for δ' because the europium compound that we used contained an insoluble fraction.

The δ' signals of the 2'- and 6'-H protons in the spectra of flavone and its derivatives coincide; this may be a consequence of averaging of the induced paramagnetic shifts because of free rotation about the C_2-C_1 bond. A qualitative examination shows that the δ'_2 and δ'_6 values may also be identical when rotation

about the C_2-C_1 bond is hindered in the case of equality of r and θ for the 2'- and 6'-H protons. It was found that the $\delta'_5/\delta'_{2,6'}$ ratio in the spectrum of the flavone is greater than six, as compared with three in the spectrum of 3-methoxyflavone. The $\delta'_3/\delta'_{2,6'}$ ratio for flavone is ~ 4.5 , whereas it is greater than five for 5-methoxyflavone. In addition, markedly different δ'_{OCH_3} values correspond to identical $\delta'_{2,6'}$ values in the spectra of 3- and 5-methoxyflavones. The signals of the 3'-, 4'-, and 5-H protons of flavone and its 3- and 5-methoxy derivatives are shifted approximately identically when $Eu(DPM)_3$ is added to the investigated samples. At the same time, the δ' values of the signals of the protons of the A ring proved to be different; this difference is expressed to a lesser degree for flavone. One's attention is drawn to the fact that $\delta'_8 > \delta'_7$ and δ'_8 in the spectrum of 3-methoxyflavone (Fig. 1, spectrum B).

It follows from a comparison of the observed paramagnetic shifts and the values expected on the basis of a qualitative examination of Stuart models with allowance for the angular factor and the distance from the coordinating ion to the resonating nuclei that the conditions for coordination do not change on passing from flavone to its 3- and 5-methoxy derivatives. The above-noted differences in the absolute and relative values of the observed paramagnetic shifts of flavones can therefore be ascribed to the different relative orientations of the A, B, and C rings. We also noted these peculiarities in the geometrical structures of the investigated compounds during an investigation of the physicochemical properties of 3- and 5-hydroxyflavones.

EXPERIMENTAL

The physicochemical constants and methods for the synthesis of the compound listed in Table 1 were presented in [4, 6, 7]. The PMR spectra of CCl_4 solutions of the compounds were recorded with a BS487B spectrometer with hexamethyldisiloxane as the internal standard (δ scale).

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