Communications to the Editor

[Chem. Pharm. Bull.]
33(1) 444-447 (1985)

DETERMINATION OF C-6 OR C-8 SUBSTITUTED FLAVANONE USING ^{13}C - ^1H LONG
RANGE COUPLING AND THE REVISED STRUCTURES OF SOME FLAVANONES

Yoshiaki Shirataki,* Ichiro Yokoe, Masaaki Endo and Manki Komatsu
Faculty of Pharmaceutical Sciences, Josai University, Keyakidai,
Sakado, Saitama 350-02, Japan

C-6 or C-8 substituted flavanones were determined by methods of chemical and/or ^1H -NMR spectral analysis. We report a very convenient method for determining the substituted position of these flavanones using ^{13}C - ^1H long range coupling. In connection with this study, we revised some structures of flavanones using this technique.

KEYWORDS ——— ^{13}C -NMR; gated decoupling with NOE; ^{13}C - ^1H long range coupling; long range selective proton decoupling (LSPD); sophoraflavanone A; sophoraflavanone B; euchrestaflavanone A; euchrestaflavanone B; euchrestaflavanone C

There are many 5,7-dihydroxyflavanones having 3,3-dimethylallyl (prenyl) or (E)-3,7-dimethyl-2,6-octadienyl (geranyl) side chains at C-6 or C-8. Some techniques have been reported to determine the substituted positions, for instance Gibbs test,¹⁾ anomalous AlCl_3 induced UV shift,²⁾ cyclized reaction,³⁾ chemical shift of $\text{C}_5\text{-OH}$,⁴⁾ or vinyl methyl proton signals in the 3,3-dimethylallyl group⁵⁾ in the ^1H -NMR spectra, and upfield shift of the ^1H -NMR spectra about benzyl protons⁶⁾ or chromene protons⁷⁾ after acetylation of $\text{C}_5\text{-OH}$. We also reported the chemical shift in ^{13}C -NMR spectra.⁸⁾ But these are not complete techniques, because the position of C-6 and C-8 may be interconverted during the chemical reaction by a Wessely-Moser rearrangement and the chemical reactions require large samples. In the NMR spectrum, the signals of $\text{C}_6\text{-H}$ and $\text{C}_8\text{-H}$ or C-6 and C-8 are very close together in 5,7-dihydroxyflavanones.

The signals of $\text{C}_6\text{-H}$ and $\text{C}_8\text{-H}$ in naringenin appear at about δ 6.0 ppm in the ^1H -NMR spectrum overlapping each other, and in the ^{13}C -NMR spectrum, C-6 appears at about δ 97 ppm and C-8 at about δ 96 ppm (in CD_3COCD_3), very near each other. So it is very difficult to determine the position of the side chain located at C-6 or C-8 in 5,7-dihydroxyflavanones by comparing them with naringenin in the ^1H -NMR spectra or by complete decoupling or off-resonance decoupling in the ^{13}C -NMR spectra.

Recently, ^{13}C - ^1H long range coupling and a technique of long range selective proton decoupling (LSPD) have been reported.⁹⁾ These are very useful in determining the substitution pattern of polysubstituted aromatic compounds. Here we describe the structural determination of C-6 or C-8 substituted flavanone using ^{13}C - ^1H long range coupling, and revise the structures of sophoraflavanone A, B, and euchrestaflavanone A, B and C.

We studied the ^{13}C - ^1H long range coupling of C-6 and C-8 with $\text{C}_6\text{-H}$, $\text{C}_8\text{-H}$ and

Table I. ^{13}C -NMR Spectral Data and LSPD Experiments for Flavanones (in CD_3COCD_3)

Compounds No.	a)										b)	
	1	3	5	4	7	9	11	10				
Formula	$\text{C}_{15}\text{H}_{12}\text{O}_5$	$\text{C}_{25}\text{H}_{28}\text{O}_5$	$\text{C}_{20}\text{H}_{20}\text{O}_5$	$\text{C}_{20}\text{H}_{20}\text{O}_5$	$\text{C}_{25}\text{H}_{28}\text{O}_5$	$\text{C}_{25}\text{H}_{28}\text{O}_6$	$\text{C}_{25}\text{H}_{26}\text{O}_6$	$\text{C}_{25}\text{H}_{26}\text{O}_6$				
mp ($^{\circ}\text{C}$)	248-251	144-145	193-195	209-210	145-147	188-190	198-200	194				
Carbons	6 8	6 8	6 8	6 8	6 8	6 8	6 8	6 8				
δ (ppm)	96.8	96.3	96.2	108.2	109.0	95.3	96.3	108.2	108.4	96.3	108.2	109.0
M	ddd	dd	dd	m	m	d	dd	m	dd	m	m	d
J	161.9	160.9	160.9	163.0	160.9	159.8	160.8	161.9				
(Hz)	(H_6) 7.3 ($\text{C}_5\text{-OH}$) 4.2 (H_8)	(H_6) 7.3 ($\text{C}_5\text{-OH}$) (H_8)	(H_6) 7.3 ($\text{C}_5\text{-OH}$) (H_8)	(H_6) 7.2 ($\text{C}_5\text{-OH}$) (H_8)	(H_6) 7.2 ($\text{C}_5\text{-OH}$) (H_8)	(H_6) 7.3 ($\text{C}_5\text{-OH}$) (H_8)	(H_6) 7.2 ($\text{C}_5\text{-OH}$) (H_8)	(H_6) 7.2 ($\text{C}_5\text{-OH}$) (H_8)				

LSPD of $\text{C}_5\text{-OH}$												
M	dd	dd	d	m	d	m	m	d	d	m	d	d
J	161.9	164.0	157.9	160.9	162.5	161.9	159.8	161.9	159.9	159.9	159.9	159.9
(Hz)	(H_6) 4.2 (H_8)	(H_8) 4.2 (H_6)	(H_6) 4.2 (H_8)	(H_6) 4.2 (H_8)	(H_8) 4.2 (H_6)	(H_8) 4.2 (H_6)	(H_8) 4.2 (H_6)	(H_6) 4.2 (H_8)	(H_6) 4.2 (H_8)	(H_6) 4.2 (H_8)	(H_6) 4.2 (H_8)	(H_8) 4.2 (H_6)

a) See ref. 10.
 b) See ref. 11.
 ^1H - and ^{13}C -NMR spectra were obtained on a JEOL JNM GX-270 FT instrument at 25°C , spectral width 4.5 (^1H) and 16 kHz (^{13}C), data points 16 kW, repetition time 6 (^1H) and 2.0-5.0 s (^{13}C), pulse width 10 (^1H) and 4.5 μs (^{13}C) (both 45° pulse), power level for LSPD 5.9 kHz, -35 dB with power attenuator.
 δ : downfield from TMS, M: multiplicity, m: unresolved multiplet.

C₅-OH using the techniques of gated decoupling with NOE and LSPD of naringenin (1).

The signal of C-6 at δ 96.8 ppm was a split double double doublet ($J=161.9, 7.3, 4.2$ Hz) and C-8 at δ 95.8 ppm was a split double doublet ($J=164.0, 4.2$ Hz). The signal of C-6 was changed into a double doublet ($J=161.9, 4.2$ Hz) and that of C-8 was not changed after LSPD of C₅-OH. Next, the signal of C-6 was changed into a doublet ($J=7.3$ Hz) and that of C-8 was changed into a singlet after LSPD of C_{6,8}-H.

This means that C-6 is coupled with C₆-H ($J=161.9$ Hz), C₈-H ($J=4.2$ Hz) and C₅-OH ($J=7.3$ Hz), and C-8 is coupled with C₈-H ($J=164.0$ Hz) and C₆-H ($J=4.2$ Hz).

Consequently, in flavanones having a side chain at C-6, the signal of C-8 is only a doublet ($J=164.0$ Hz) coupled with C₈-H at about δ 95 ppm and is not changed after LSPD of C₅-OH. In another case, having a side chain at C-8, the C-6 signal is a double doublet ($J=161.9, 7.3$ Hz) coupled with C₆-H and C₅-OH at about δ 96 ppm and changed to a doublet ($J=161.9$ Hz) coupled with only C₆-H after LSPD of C₅-OH.

We have reported that the structures of sophoraflavanone A (2),⁸⁾ B (4),¹²⁾ euchrestaflavanone A (6),¹³⁾ B (8)¹⁴⁾ and C (10),¹⁴⁾ have a side chain at C-6, as determined by Gibbs test¹⁵⁾ and the chemical shifts of ¹³C-NMR spectra. But the present investigation (Table I) lead to a revision to a C-8 substitution of the side chains (3,5,7,9 and 11) (Fig. 1).

Fig. 1

Earlier, Byrne *et al.*¹⁶⁾ used the long range coupling technique without LSPD for the structural elucidation of (+)-cryptostrobin, (+)-strobopin, (+)-lawinal, unonal, 7-O-methylunonal and isounonal. We have applied the LSPD technique widely to prenyl and geranyl side chains, and have established the usefulness of this technique. Since the structures of C₆ or C₈ substituted flavanones have been so confusing, the ¹³C-¹H long range coupling and LSPD methods should be very useful in their analysis.

ACKNOWLEDGEMENT We are grateful to Prof. T. Nomura, Faculty of Pharmaceutical Sciences, Toho University and to Dr. S. Mizobuchi, Applied Bioscience Laboratory, Kirin Brewery Co., Ltd., for their kind donation of the data on cudraflavanone A, 6-prenylnaringenin and 8-prenylnaringenin, and for useful discussion regarding the determination of these flavanones. Thanks are also due to Mr. S. Yamaguchi, Josai University, for the NMR spectral measurements.

REFERENCES AND NOTES

- 1) C. P. Rao, V. S. S. Vemuri and K. V. Jagannadha Rao, *Indian J. Chem.*, **21B**, 167 (1982).
- 2) E. A. Sherif, R. K. Gupta and M. Krishnamurti, *Tetrahedron Letters*, **21**, 641 (1980).
- 3) A. C. Jain, R. C. Gupta and P. D. Sarpal, *Tetrahedron*, **34**, 3563 (1978).
- 4) F. Bohlmann, C. Zdero, H. Robinson and R. M. King, *Phytochemistry*, **20**, 2245 (1981).
- 5) F. Bohlmann and C. Zdero, *Phytochemistry*, **22**, 2877 (1983).
- 6) K. Yakushijin, K. Shibayama, H. Murata and H. Furukawa, *Heterocycles*, **14**, 397 (1980).
- 7) T. M. Smalberger, R. Vleggaar and J. C. Weber, *Tetrahedron*, **30**, 3927 (1974).
- 8) Y. Shirataki, M. Endo, I. Yokoe and M. Komatsu, *Chem. Pharm. Bull.*, **31**, 2859 (1983), and references cited therein.
- 9) H. Komura, K. Mizukawa, H. Minakata, H. Huang, G. Qin and R. Xu, *Chem. Pharm. Bull.*, **31**, 4206 (1983).
- 10) 8-prenylnaringenin was reported earlier by Bohlmann *et al.*, but the analysis was based only on IR, MS and ^1H -NMR spectra, and the compound was not in crystal form. *Phytochemistry*, **18**, 1246 (1979). Dr. S. Mizobuchi informed us that he isolated 6-prenylnaringenin from *Humulus lupulus* (Moraceae). *Agric. Biol. Chem.*, **48**, 2771 (1984). Direct comparisons of 6-prenylnaringenin isolated from *Humulus lupulus* have been made by Mizobuchi and we have synthesized it. We also compared 8-prenylnaringenin synthesized by Mizobuchi with sophoraflavanone B which we isolated from *Sophora tomentosa*, and their structures have been confirmed by all of us.
- 11) Cudraflavanone A (10), the former structure of euchrestaflavanone C, has been isolated by T. Fujimoto and T. Nomura from *Cudrania tricuspidata* (Moraceae). *Heterocycles*, **22**, 997 (1984).
- 12) M. Komatsu, I. Yokoe and Y. Shirataki, *Chem. Pharm. Bull.*, **26**, 3863 (1978).
- 13) Y. Shirataki, M. Komatsu, I. Yokoe and A. Manaka, *Chem. Pharm. Bull.*, **29**, 3033 (1981).
- 14) Y. Shirataki, A. Manaka, I. Yokoe and M. Komatsu, *Phytochemistry*, **21**, 2959 (1982).
- 15) H. D. Gibbs, *J. Biol. Chem.*, **72**, 649 (1927); F. E. King, T. J. King and L. C. Manning, *J. Chem. Soc.*, **1957**, 563.
- 16) L. T. Byrne, J. R. Cannon, D. H. Gawad, B. S. Joshi, B. W. Skelton, R. F. Toia and A. H. White, *Aust. J. Chem.*, **35**, 1851 (1982).

(Received November 16, 1984)