# REVISED STRUCTURE OF A NATURAL FLAVONE FROM ARTEMISIA LANATA

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Key Word Index—Artemisia lanata; Compositae, 5,3'-dihydroxy-3,6,7,4'-tetramethoxyflavone, 5,4'-dihydroxy-3,6,7,3'-tetramethoxyflavone; 3,5-dihydroxy-7,8,3',4'-tetramethoxyflavone, revised structure.

Abstract—The structure of a natural flavone from Artemisia lanata, thought to be 3,5-dihydroxy-7,8,3',4'-tetramethoxyflavone, is revised to 5,3'-dihydroxy-3,6,7,4'-tetramethoxyflavone on the basis of spectral data.

#### INTRODUCTION

We have recently established a new convenient method for the synthesis of 3,5-dihydroxy-7,8-[1, 2] and 6,7dioxygenated flavones [3] and clarified their spectroscopic properties. A natural flavone reported as 3,5dihydroxy-7,8,3',4'-tetramethoxyflavone (1) [4], does not show the expected properties for 3,5-dihydroxy-7,8dimethoxyflavones. This structure is here revised to 5,3'dihydroxy-3,6,7,4'-tetramethoxyflavone (2), casticin.

### **RESULTS AND DISCUSSION**

The structure of a natural flavone, isolated from Artemisia lanata along with artemetin (5-hydroxy-3.6.7.3'.4'pentamethoxyflavone) and 5-hydroxy-6,7,3',4'-tetramethoxyflavone, was proposed as 1 by Esteban et al. [4], but the UV spectral data differ from those for the synthetic flavone 1 [1]. For example, Band I occurs at a shorter wavelength than that in 3-hydroxyflavones [1, 2,3, 5], suggesting that the natural flavone lacks a free hydroxy group at the 3-position. The singlet at  $\delta 6.87$  in the <sup>1</sup>HNMR for the acetate of the natural flavone appeared at a lower field than is known for 3,5dihydroxy-7,8-dimethoxyflavones [1], suggesting that the signal should be assigned to the  $C_8$ -proton in a 5,6,7trioxygenated flavone having a methoxy group at the 7position [3]. Thus, the Artemisia compound must be a 3,5,6,7,3',4'-hexaoxygenated flavone having methoxy groups at the 3- and 7-positions.

Esteban *et al.* reported that the natural flavone was synthesized along with 3,5-dihydroxy-6,7,3',4'-tetramethoxyflavone (3) by demethylation of artemetin with hydrochloric acid and the flavone 3 was also obtained by the demethylation with dry aluminum chloride in ether [4]. According to our experience, the 3-methoxy group in artemetin is difficult to cleave [6] and demethylation takes place sequentially at the 6-, 4'-, and 3'-positions [6–8]. Therefore, we re-examined the demethylation of artemetin by TLC and confirmed the above demethylation sequence. Only 5,6-dihydroxy-3,7,3',4'-tetramethoxyflavone (4) was obtained on demethylation of artemetin with dry aluminum chloride in ether; 5,4'dihydroxy-3,6,7,3'-tetramethoxyflavone (5) and 5,3'dihydroxy-3,6,7,4'-tetramethoxyflavone (2) were detected with 4 on demethylation with hydrochloric acid in acetic acid. The properties of the flavones, 2 and 5, are similar to those of the flavone, proposed as 3 by Esteban et al, suggesting that original flavone is 2 or 5. The two isomeric flavones, 2 and 5, are easily distinguishable by differences in their spectral data (Table 1). Thus the original flavone is 2, and the spectral data for the natural product and its acetate are identical with those for 2 and its acetate as shown in Table 1 In an earlier study, a flavone isolated from Artemisia annua, was assumed to be 3 [9] but it was later revised to 5 by Bhardwaj et al. [10]. However, it is clear from the published spectral data (Table 1) that it has not been properly destinguished from 2 and hence its structure is still not absolutely certain

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					N H <sub>1</sub>	MR IN CDC	Л <sub>3</sub> (д)		I.	HNMR for	acetate in C	:DCl <sub>3</sub> (δ)	
Compound (Mp °)		UV. $\lambda_{max}n_1$ (AlCl <sub>3</sub> )	n (NaOAc)	C <sub>8</sub> - or C <sub>6</sub> -H	С,-Н	C <sub>2</sub> -H OMe	C, -H	HO	C <sub>8</sub> - or C <sub>6</sub> -H	С,-Н	C <sub>2</sub> H OMe	C <sub>6</sub> -H	OAc
1 (3,5-OH-7,8,3',4'-OMe) (219-219 5)	(EtOH)384 337 275sh 257	443 363 267	425 1 400 335 258	6 45 <i>s</i> 3.95 <i>s</i>	703 d 395 s	7.88 <i>d'</i> 3 97 s	793 dd 398 s	11 57 s	6 61 s 3 90 s	692 d 392 s	741 d' 392 s	7 49 <i>dd</i> 3 92 s	2 32 <i>s</i> 2 40 <i>s</i>
Natural flavone (178–180)	(MeOH)345 270 256	378 279 270	345 270 256	647 <i>s</i> 384 <i>s</i>	693 <i>d</i> 389 <i>s</i>	7.61 d' 3 93 s	7 64 dd 3 96 s	12 57 s	687 s 377 s	7 04 d 3 83 s	7 76 ď 3 89 s	8 00 dd 3 95 s	2 34 s 2 49 s
2† (5,3'-OH-3,6,7,4'-OMe) (183 5-184)	(EtOH)351 270 258	360 270 1 262	351 270 259	6 43 <i>s</i> 3 83 <i>s</i>	687 d 387 s	7 60 <i>d'</i> 3 90 s	7 64 dd 3 93 s	1247s	6 79 s 3 76 s	6.99 d 3 80 s	7 70 d' 3 86 s	7 94 dd 3 93 s	2.32 s 2.48 s
5† (5,4'-OH-3,6,7,3'-OMe) (180,5181)	(EtOH)353 271 258	367 278 266	420 360 261	6.42 <i>s</i> 3 81 <i>s</i>	695 <i>d</i> 387 <i>s</i>	7 63 <i>d'</i> 3 90 <i>s</i>	7 59 dd 3 93 s	1241 \$	6 79 s 3 78 s	7 10 d 3 82 s	7.67 d' 3 87 s	7 59 dd 3 94 s	2 32 s 2 48 s
<b>3</b> (3,5-OH-6,7,3′,4'-OMe) (235-235 5)	(EtOH)366 271 258	421 382sh 265	415 1 370 270 1 258	6 57 s 3 94 s	7 01 <i>d</i> 3 98 s	7 80 <i>d'</i> 3 99 s	7 83 dd 4 00 s	11 68 5	6 82 s 3.80 s	6 89 <i>d</i> 3.90 <i>s</i>	7 29 ď 3 90 s	7 38 dd 3 93 s	2 29 s 2 45 s
3 synthesized by Esteban et al (210–212)	(MeOH)345 278 258	378 290 260	355 278	6 54 s 3 86 s	6.98 d 3 97 s	7 64 ď 3 97 s	7 70 dd 4 00 s	12 40 \$	679 s 371 s	692 <i>d</i> 387 <i>s</i>	7 57 d' 3 90 s	7 61 <i>dd</i> 3 90 s	2 28 s 2 40 s
<b>4</b> (5,6-OH-3,7,3',4'-OMe) (220-222)	(EtOH)347 283 255 1	374 296 260	343 285	655 s 391 s	695 <i>d</i> 401 <i>s</i>	7 <i>67 d</i> ' 401 s	772 dd 403 s	12 38 s	6 86 s 3 78 s	694 <i>d</i> 391 <i>s</i>	7 62 d' 3 93 s	7 66 <i>dd</i> 3 93 s	2 32 s 2 45 s
Natural flavone (3) Djermanovic et al (171-172)	(MeOH)352 265 210	390 272 210	403‡ 272‡ 210‡	6 50 s 3 89 s	701 d 395 s	7 70 m(2) 3 98 s	H) 4 00 s						

10% Pd-C in methanol-ethyl acetate respectively.  $\ddagger A$  set of data is in the presence of sodium methoxide. The corresponding  $\dot{\lambda}_{max}$  for 2 and 5 are 391, 272 nm and 415, 271 nm, respectively

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## FLAVONOIDS FROM SALVIA TEXANA

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Abstract—From a methanolic root extract of Salvia texana, 5-hydroxy-7,4'-dimethoxyflavone and (+)-2(S)-5hydroxy-7-methoxyflavanone were isolated and characterized by spectroscopy. The absolute configuration of the latter compound was established by CD readings

In the course of our study of secondary metabolites with biological activity from the medicinal flora of Latin America, various new aromatic diterpenes have been isolated from the roots of Salvia texana [1, 2] and 5hydroxy-7,4'-dimethoxyflavone (1) and (+) 2(S)-5-hydroxy-7-methoxyflavanone (2) from the same source have now been identified.

Compound 1 was isolated as a yellow crystalline solid with the molecular formula  $C_{17}H_{14}O_5$  (HRMS). In its IR spectrum bands for phenol  $(3650 \text{ cm}^{-1})$ , a conjugated carbonyl (1650 cm<sup>-1</sup>) and ether (1250 and  $1030 \text{ cm}^{-1}$ ) were observed. The UV spectrum and the <sup>1</sup>HNMR in pyridine- $d_6$  confirmed that 1 is a flavone with a free phenol group and two methoxyl groups. A one-proton singlet at  $\delta$  13.60 exchangeable with D<sub>2</sub>O and assigned to the phenolic proton bridged to the carbonyl suggested that the free phenol group was at C-5. A fragment at m/z122 (hydroxyanisol ion) in the MS spectrum [3] together with two broad one-proton singlets at  $\delta 6.62$  and 6.70 in <sup>1</sup>H NMR for meta H-6 and H-8, placed one of the methoxyl groups at C-7. Fragments at m/z 132 and 135 in the MS and two doublets of two protons each at  $\delta 7.12$ and 7.96, respectively, sited the other methoxyl group on C-4'. These data and the <sup>13</sup>C NMR (Table 1) confirmed the structure of 1 as 5-hydroxy-7,4'-dimethoxyflavone. The physical and <sup>1</sup>H NMR data coincided with those of di-O-methylapigenin isolated from Sideritis gomerae Bolle [4].

Compound 2 proved to be a new flavanone the structure and absolute configuration of which were established from the following: the MS spectrum showed the molecu-

Table	1.	<sup>13</sup> C NMR data of 1 (CDCl <sub>3</sub> )	
		(50 MHz)	

С		С	
2	162.4	10	105.2
3	104.5	1′	123.8
4	182.5	2'	128.1
5	1574	3′	114.6
6	98.1	4'	162 5
7	165 6	5'	114.6
8	92.7	6'	128.1
9	162 0	7-OMe	55.5*
		4'-OMe	55 7*

\*Interchangeable values.

lar 10n at m/z 270,  $C_{16}H_{14}O_4$  (HRMS); the IR spectrum had bands for phenol (3650 cm<sup>-1</sup>), conjugated carbonyl (1630 cm<sup>-1</sup>) and ether (1040 cm<sup>-1</sup>). In the <sup>1</sup>H NMR spectrum, a single methyl group was seen as a singlet at  $\delta$ 3.81. A one-proton singlet at  $\delta$ 11.5, interchangeable with  $D_2O_2$ , sited the free phenol group at C-5 with a bridge to the carbonyl. A broad two-proton singlet at  $\delta 6.07$ attributable to meta H-6 and H-8, together with a fragment at m/z 193 in MS (generated by the loss of the Bring), placed the methoxyl group on C-7. A five-proton multiplet at  $\delta$ 7.44 confirmed the non-substitution of the B-ring. The most characterized feature of the <sup>1</sup>H NMR was the absence of the typical flavone H-3 proton and the