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The <sup>13</sup>C-nmr spectra of various methyl derivatives of angelicin are reported. The assignment of chemical shifts for all the C atoms has been achieved by using carbon-proton coupling constants, nuclear Overhauser effect consideration and shift effects caused by the introduction of methyl groups on various positions of the angelicin nucleus. Substituent effects on <sup>13</sup>C chemical shifts and carbon-proton coupling constants are discussed.

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### Introduction.

Many <sup>13</sup>C-nmr studies concerning coumarinoids are available in literature since the Carbon-13 Pulse Fourier Transform NMR Spectroscopy has become common as a sensitive and powerful tool in structural elucidation as well as in studies of chemical conformation [2]. However, the majority of these studies regard natural and synthetic

coumarin derivatives, while little is done concerning furocoumarin derivatives, annulated both linearly [3-5] and angularly [6].

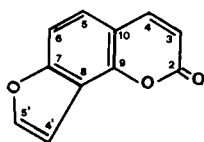
On the other hand, great attention is given at present to furocoumarins, owing to their interesting photobiological properties, connected with their ability to photoreact with the DNA macromolecule [7-9].

Table 1

<sup>13</sup>C-NMR Spectra of Various Methylangelicins

	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-4'	C-5'	3-Me	4-Me	5-Me	6-Me	4'-Me	5'-Me
Ang	160.7	114.1	144.5	123.8	108.8	157.3	116.9	148.5	113.5	104.0	145.9						
3 [a]	162.2	123.1	140.2	123.0	108.5	156.6	116.6	147.3	114.1	103.9	145.6	17.1					
4	160.7	112.8	153.6	120.5	108.3	157.2	116.9	147.9	114.5	104.3	145.8		19.4				
5	160.6	113.5	141.3	132.2	109.6	157.3	115.1	149.1	112.7	104.0	145.0			18.9			
6	161.1	114.0	144.5	123.7	119.1	156.7	116.3	146.9	113.6	104.4	145.6				14.6		
4'	160.4	113.7	144.4	123.7	108.7	157.9	117.4	149.8	113.4	115.9	142.3					9.4	
5'	161.0	113.8	144.6	122.7	108.1	157.1	118.3	147.6	113.4	99.9	156.8						14.1
3,4	161.8	119.7	147.0	120.3	108.0	156.3	116.5	147.0	114.9	104.1	145.4	13.3	15.6				
3,4'	162.1	122.8	140.3	122.9	108.5	157.1	117.2	148.7	114.0	115.8	142.0	17.1				9.6	
3,5'	162.3	122.7	140.4	121.8	107.9	156.3	117.9	146.6	114.0	99.8	156.4	17.0					14.0
						[b]					[b]						
4,6	161.1	112.7	153.5	120.4	118.6	156.2	116.3	146.4	114.6	104.6	145.5		19.4		14.9		
4,4'	160.4	112.5	153.3	120.3	108.2	157.9	117.4	149.4	114.3	116.2	142.2		19.2			9.5	
4,5'	160.8	112.7	153.5	119.3	107.7	157.1	118.5	147.2	114.5	100.2	156.7		19.2				14.0
5,6	160.9	113.2	141.9	129.5	117.4	156.7	114.0	147.2	112.8	104.3	144.8			14.2	12.0		
5,4'	160.4	113.0	141.2	132.0	109.5	157.8	115.5	150.3	112.4	115.9	141.4			18.8		9.4	
5,5'	161.0	113.0	141.5	130.9	109.1	157.0	116.4	148.1	112.5	99.8	155.8			18.8			14.0
6,4'	161.0	113.5	144.5	123.5	119.0	156.8	116.7	148.2	113.3	116.2	142.0				14.5	9.5	
6,5'	161.2	113.5	144.5	122.6	118.4	156.0	117.5	146.0	113.3	100.1	156.4				14.6		14.1
4',5'	160.9	113.3	144.6	122.4	108.0	156.2	118.4	148.8	113.3	109.8	151.7					9.5	11.6
3,4,4'	161.6	119.4	146.9	120.1	108.0	156.9	116.9	147.4	114.8	116.0	141.9	13.3	15.6			9.7	
3,4,5'	162.1	119.4	147.2	119.0	107.4	156.1	118.0	145.2	114.9	100.0	156.3	13.3	15.6				14.1
						[b]					[b]						
4,6,4'	161.1	112.5	153.5	120.3	118.5	156.8	116.8	147.7	114.4	116.5	141.9		19.5		14.8	9.7	
						[b]				[b]							
4,6,5'	161.3	112.4	153.6	119.3	118.0	156.0	117.7	145.6	114.4	100.4	156.3		19.4		14.8		14.2
5,6,4'	160.8	112.7	141.8	129.2	117.2	157.1	114.4	148.5	112.5	116.1	141.2			14.1	11.7	9.6	
5,6,5'	161.1	112.7	141.9	128.3	116.7	156.3	115.2	146.2	112.5	100.0	155.4			14.0	11.8		14.0
4,4',5'	160.7	112.1	153.5	118.9	107.4	156.0	118.2	148.1	114.1	109.9	151.5		19.3			9.5	11.5

[a] The numbers indicate the positions of the methyl groups in the Angelicin molecule. [b] The corresponding values may be interchanged.



I

In this connection we have recently prepared a number of angularly annulated furocoumarin derivatives, *i.e.* methyl derivatives of angelicin [10] and we have demonstrated their ability to photobind to DNA giving for geometrical reasons only monofunctional adducts [11,12].

The availability of the complete series of monomethyl-

angelicins, in addition to a number of di- and trimethylangelicins led us to perform a  $^{13}\text{C}$ -nmr study on these compounds, affording convincing attributions of chemical shifts which confirm the assignments previously given for angelicin and some of its 5' derivatives by the use of chemical shift reagents [6].

In the present work much reliance has therefore been placed on the internal consistency of shift changes following substitutions and on the use of coupling constant data.

In addition, the substituent chemical shifts for these compounds has also been considered, demonstrating that the methyl substituent effects obey quite precise rules with a few exceptions, that is when two methyl groups are located in a vicinal situation.

Table 2  
Substituent Chemical Shifts Values for the Methylangelicins

	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-4'	C-5'
3	+1.5	+9.0	-4.3	-0.8	-0.3	-0.7	-0.3	-1.2	+0.6	-0.1	-0.3
4	0.0	-1.3	+9.1	-3.3	-0.5	-0.1	0.0	-0.6	+1.0	+0.3	-0.1
5	-0.1	-0.6	-3.2	+8.4	+0.8	0.0	-1.8	+0.6	-0.8	0.0	-0.9
6	+0.4	-0.1	0.0	-0.1	+10.3	-0.6	-0.6	-1.6	+0.1	+0.4	-0.3
4'	-0.3	-0.4	-0.1	-0.1	-0.1	+0.6	+0.5	+1.3	-0.1	+11.9	-3.6
5'	+0.3	-0.3	+0.1	-1.1	-0.7	-0.2	+1.4	-0.9	-0.1	-4.1	+10.9
3,4	+1.1	+5.6	+2.5	-3.5	-0.8	-1.0	-0.4	-1.5	+1.4	+0.1	-0.5
	(+1.5)	(+7.7) [b]	(+4.8) [b]	(-4.1) [a]	(-0.8)	(-0.8)	(-0.3)	(-1.8)	(+1.6)	(+0.2)	(-0.4)
3,4'	+1.4	+8.7	-4.2	-0.9	-0.3	-0.2	+0.3	+0.2	+0.5	+11.8	-3.9
	(+1.2)	(+8.6)	(-4.4)	(-0.9)	(-0.4)	(-0.1)	(+0.2)	(+0.1)	(+0.5)	(+11.8)	(-3.9)
3,5'	+1.6	+8.6	-4.1	-2.0	-0.9	-1.0 or -0.9	+1.0	-1.9	+0.5	-4.2	+10.4 or +10.5
	(+1.8)	(+8.7)	(-4.2)	(-1.9)	(-1.0)	(-0.9)	(+1.1)	(-2.1)	(+0.5)	(-4.2)	(+10.6)
4,6	+0.4	-1.4	+9.0	-3.4	+9.8	-1.1	-0.6	-2.1	+1.1	+0.6	-0.4
	(+0.4)	(-1.4)	(+9.1)	(-3.4)	(+9.8)	(-0.7)	(-0.6)	(-2.2)	(+1.1)	(+0.7)	(-0.4)
4,4'	-0.3	-1.6	+8.8	-3.5	-0.6	+0.6	+0.5	+0.9	+0.8	+12.2	-3.7
	(-0.3)	(-1.7)	(+9.0)	(-3.4)	(-0.6)	(+0.5)	(+0.5)	(+0.7)	(+0.9)	(+12.2)	(-3.7)
4,5'	+0.1	-1.4	+9.0	-4.5	-1.1	-0.2	+1.6	-1.3	+1.0	-3.8	+10.8
	(+0.3)	(-1.6)	(+9.2)	(-4.4)	(-1.2)	(-0.3)	(+1.4)	(-1.5)	(+0.9)	(-3.8)	(+10.8)
5,6	+0.2	-0.9	-2.6	+5.7	+8.6	-0.6	-2.9	-1.3	-0.7	+0.3	-1.1
	(+0.3)	(-0.7)	(-3.2) [a]	(+8.3) [b]	(+11.1) [b]	(-0.6)	(-2.4) [a]	(-1.0)	(-0.7)	(+0.4)	(-1.2)
5,4'	-0.3	-1.1	-3.3	+8.2	+0.7	+0.5	-1.4	+1.8	-1.1	+11.9	-4.5
	(-0.4)	(-1.0)	(-3.3)	(+8.3)	(+0.7)	(+0.6)	(-1.3)	(+1.9)	(-0.9)	(+11.9)	(-4.5)
5,5'	+0.3	-1.1	-3.0	+7.1	+0.3	-0.3	-0.5	-0.4	-1.0	-4.2	+9.9
	(+0.2)	(-0.9)	(-3.1)	(+7.3)	(+0.1)	(-0.2)	(-0.4)	(-0.4)	(-0.9)	(-4.1)	(+10.0)
6,4'	+0.3	-0.6	0.0	-0.3	+10.2	-0.5	-0.2	-0.3	-0.2	+12.2	-3.9
	(+0.1)	(-0.5)	(-0.1)	(-0.2)	(+10.2)	(0.0) [a]	(-0.1)	(-0.3)	(0.0)	(+12.3)	(-3.9)
6,5'	+0.5	-0.6	0.0	-1.2	+9.6	-1.3	+0.6	-2.5	-0.2	-3.9	+10.5
	(+0.7)	(-0.4)	(+0.1)	(-1.2)	(+9.6)	(-0.8) [a]	(+0.8)	(-2.5)	(0.0)	(-3.7)	(+10.6)
4',5'	+0.2	-0.8	+0.1	-1.4	-0.8	-1.1	+1.5	+0.3	-0.2	+5.8	+5.8
	(0.0)	(-0.7)	(0.0)	(-1.2)	(-0.8)	(+0.4) [b]	(+1.9)	(+0.4)	(-0.2)	(+7.8) [b]	(+7.3) [b]
3,4,4'	+0.9	+5.3	+2.4	-3.7	-0.8	-0.4	0.0	-1.1	+1.3	+12.0	-4.0
	(+1.2)	(+7.3) [b]	(+4.7) [b]	(-4.2) [a]	(-0.9)	(-0.2)	(+0.2)	(-0.5) [a]	(+1.5)	(+12.1)	(-4.0)
3,4,5'	+1.4	+5.3	+2.7	-4.8	-1.4	-1.2 or -1.0	+1.1	-3.3	+1.4	-4.0	+10.4 or +10.2
	(+1.8)	(+7.4) [b]	(+4.9) [b]	(-5.2)	(-1.5)	(-1.0)	(+1.1)	(-2.7) [a]	(+1.5)	(-3.9)	(+10.5)
4,6,4'	+0.4	-1.6	+9.0	-3.5	+9.7	-0.5	-0.1 or -0.4	-0.8	+0.9	+12.5 or +12.8	-4.0
	(+0.1)	(-1.8)	(+9.0)	(-3.5)	(+9.7)	(-0.1)	(-0.1)	(-0.9)	(+1.0)	(+12.6)	(-4.0)
4,6,5'	+0.6	-1.7	+9.1	-4.5	+9.2	-1.3	+0.8	-2.9	+0.9	-3.6	+10.4
	(+0.7)	(-1.7)	(+9.2)	(-4.5)	(+9.1)	(-0.9)	(+0.8)	(-3.1)	(+1.0)	(-3.4)	(+10.5)
5,6,4'	+0.1	-1.4	-2.7	+5.4	+8.4	-0.2	-2.5	0.0	-1.0	+12.1	-4.7
	(0.0)	(-1.1)	(-3.3) [a]	(+8.2) [b]	(+11.0) [b]	(0.0)	(-1.9) [a]	(+0.3)	(-0.8)	(+12.3)	(-4.8)
5,6,5'	+0.4	-1.4	-2.6	+4.5	+7.9	-1.0	-1.7	-2.3	-1.0	-4.0	+9.5
	(+0.6)	(-1.0)	(-3.1) [a]	(+7.2) [b]	(+10.4) [b]	(-0.8)	(-1.0) [a]	(-1.9)	(-0.8)	(-3.7)	(+9.7)
4,4',5'	0.0	-2.0	+9.0	-4.9	-1.4	-1.3	+1.3	-0.4	+0.6	+5.9	+5.6
	(0.0)	(-2.0)	(+9.1)	(-4.5)	(-1.3)	(+0.3) [b]	(+1.9) [a]	(-0.2)	(+0.8)	(+8.1) [b]	(+7.2) [b]

Numbers in brackets represent the substituent chemical shift values predicted by a combination of data from monomethylangelicins. Excepting the cases [a] and [b] all differences ( $\delta$ ) between predicted and observed values are minor or equal to 0.4 ppm. [a] The corresponding differences are:  $0.5 \leq \delta \leq 0.9$  ppm; [b] The corresponding differences are:  $\delta > 1.0$  ppm.

## Results and Discussion.

Table 1 summarizes the chemical shifts of angelicin (ANG) and its methyl derivatives obtained in a conventional proton broad band decoupled mode of acquisition; Table 2 summarizes the substituent chemical shifts induced upon replacement of the various protons in angelicin by methyl groups; in Table 3 the  $^{13}\text{C}$ - $^1\text{H}$  coupling constants, obtained by retaining the proton information through gated decoupling experiments in some selected methylangelicins, have been collected.

In the spectra obtained in the proton decoupled mode of acquisition, quaternary carbons can be clearly distinguished from protonated carbons by their lower signal heights, owing to the lack of nuclear Overhauser enhancement.

The absorption of the quaternary carbon, deriving from substitution of hydrogens by methyl groups can easily be assigned because they move significantly downfield (Table 2). In fact methylated C-3 and C-4 carbons of the pyron ring show an increase in chemical shift of *ca.* 9 ppm, benz-

enoid carbons C-5 and C-6 show an increase of *ca.* 8 and 10 ppm respectively and C-4' and C-5' of the furan ring an increase of *ca.* 12 and 11 ppm respectively. In the proton coupled spectra (Table 3) these quaternary carbon signals appear as quartets with a coupling constant of 6-6.5 Hz for the pyron ring and benzenoid carbons and of 7 Hz for the furan ring carbons. Carbons *ortho* to the methylated site also show a quartet splitting of 5-6.5 Hz, with the exception of the C-2 and C-4' signals which show a splitting of *ca.* 4 Hz.

The chemical shifts of these *ortho* carbons are differently perturbed by the presence of the methyl group: the C-4' and C-5' carbons of the furan ring and the C-4 carbon of the pyron ring are displaced upfield about 4 ppm; C-2 and C-3 carbons move in an opposite way the former downfield and the latter upfield, of *ca.* 1.5 ppm; the benzenoid C-5 carbon is practically unaffected by the presence of a 6-methyl group, while the benzenoid C-6 carbon moves slightly downfield (*ca.* 1 ppm). The presence of a methyl group in the 4 or 5 position moves the shifts of the C-5 and

Table 3

 $^{13}\text{C}$ - $^1\text{H}$  Coupling Constants of Various Methylangelicins From Gated Decoupling Experiments

	[a] 6	5'	3,5'	4,4'	4,5'	5,4'
C-2	C2-H3 = 4.5 C2-H4 = 11.5	C2-H3 = 4.5 C2-H4 = 11.5	C2-H4 = 11.0 C2-3Me = 4.5	C2-H3 = 4.0	C2-H3 = 4.5	C2-H3 = 4.5 C2-H4 = 11.5
C-3	C3-H3 = 172.0	C3-H3 = 172.0	C3-3Me = 6.0	C3-H3 = 169.0 C3-4Me = 6.0	C3-H3 = 169.5 C3-4Me = 6.0	C3-H3 = 172.0
C-4	C4-H4 = 162.0 C4-H5 = 5.0	C4-H4 = 162.0 C4-H5 = 4.0 doublet 2.0 [f]	C4-H4 = 161.0 C4-H5 = 4.0 C4-3Me = 5.5	C4-H5 = 4.0 C4-4Me = 6.0	C4-H5 = 4.0 C4-4Me = 6.0	C4-H4 = 161.0
C-5	C5-H5 = 160.0 C5-H4 = 4.0 C5-6Me = 5.0	C5-H5 = 163.0 C5-H4 = 4.0	C5-H5 = 163.0 C5-H4 = 4.5	C5-H5 = 162.0	C5-H5 = 162.0	C5-H4 = 3.0 C5-5Me = 6.5
C-6	C6-6Me = 6.5	C6-H6 = 167.0	C6-H6 = 166.5	C6-H6 = 167.0	C6-H6 = 167.0	C6-H6 = 164.5 C6-5Me = 6.0
C-7	[b]	[e]	[e]	C7-H5 = 9.5 C7-H5' = 8.0	[e]	C7-H5' = 8.0 [d]
C-8	C8-H4' = 4.0 C8-H5' = 6.5	[e]	C8-H6 = 4.0 C8-H4' = 4.5	C8-H6 = 4.0 C8-H5' = 6.5	C8-H6 = 4.0 C8-H4' = 4.0	C8-H6 = 4.0 C8-H5' = 6.5
C-9	[b]	C9-H4 = 6.0 C9-H5 = 7.5 [d]	C9-H4 = 6.0 C9-H5 = 7.5	C9-H5 = 7.5	C9-H5 = 7.5 [d]	C9-H4 = 6.0 [d]
C-10	C10-H3 = 8.0 [d]	[c]	C10-H6 = 7.0 [d]	[c]	[c]	[c]
C-4'	C4'-H4' = 181.5 C4'-H5' = 13.5	C4'-H4' = 179.5 C4'-5'Me = 4.0	C4'-H4' = 178.5 C4'-5'Me = 4.0	C4'-H5' = 13.5 C4'-4'Me = 7.0	C4'-H4' = 179.5 C4'-5'Me = 4.0	C4'-H5' = 13.5 C4'-4'Me = 7.0
C-5'	C5'-H5' = 204.0 C5'-H4' = 10.5	C5'-H4' = 10.5 C5'-5'Me = 7.0	[e]	C5'-H5' = 201.5 C5'-4'Me = 6.5	C5'-H4' = 10.5 C5'-5'Me = 7.0	C5'-H5' = 201.5 C5'-4'Me = 6.5
3-Me			C-H = 129.0 3Me-H4 = 5.0			
4-Me				C-H = 128.5 4Me-H3 = 5.5	C-H = 128.5 4Me-H3 = 5.5	
5-Me						C-H = 127.0 5Me-H6 = 5.0
6-Me	C-H = 128.5 6Me-H5 = 5.0					
4'-Me				C-H = 129.0 4'Me-H5' = 1.5		C-H = 129.0 4'Me-H5' = 1.5
5'-Me		C-H = 129.0 [d]	C-H = 129.5		C-H = 129.0 5'Me-H4' = 1.0	

Table 3, Continued

	[a] 6,4'	6,5'	4,5'	4,6,5'	5,6,5'	4,4',5'
C-2	C2-H3 = 4.5 C2-H4 = 11.5	C2-H3 = 4.5 C2-H4 = 11.5	C2-H3 = 4.5 C2-H4 = 11.5	C2-H3 = 4.0	C2-H3 = 4.5 C2-H4 = 11.5	C2-H3 = 4.0
C-3	C3-H3 = 171.5	C3-H3 = 172.0	C3-H3 = 172.0	C3-H3 = 169.0 C3-4Me = 5.5	C3-H3 = 172.0	C3-H3 = 169.0 C3-4Me = 6.0
C-4	C4-H4 = 162.0 C4-H5 = 5.0	C4-H4 = 162.0 C4-H5 = 5.0	C4-H4 = 162.0 C4-H5 = 3.0 doublet 2.5 [f]	C4-H5 = 4.0 C4-4Me = 6.0	C4-H4 = 161.0	C4-H5 = 4.0 C4-4Me = 6.0
C-5	C5-H5 = 161.0 C5-H4 = 4.0 C5-6Me = 5.0	C5-H5 = 161.0 C5-H4 = 4.0 C5-6Me = 5.0	C5-H5 = 163.5 C5-H4 = 4.0	C5-H5 = 159.0 C5-6Me = 5.5	[c]	C5-H5 = 162.0
C-6	C6-6Me = 6.0	C6-6Me = 6.5	C6-H6 = 166.5	C6-6Me = 6.5	C6-5Me = 6.0 C6-6Me = 6.0	C6-H6 = 166.5
C-7	[c]	[e]	C7-H5 = 10.0 doublet 6.0 [f] doublet 6.0 [f]	[e]	[c]	C7-H5 = 9.5
C-8	C8-H5' = 6.5	C8-H4' = 4.5 [d]	C8-H6 = 4.0 [d]	C8-H4' = 4.5 [d]	C8-H4' = 4.5 [d]	C8-H6 = 4.0 [d]
C-9	C9-H4 = 6.0 C9-H5 = 7.5	C9-H4 = 7.0 C9-H5 = 9.0 [d]	C9-H4 = 6.0 C9-H5 = 7.5	C9-H5 = 9.0	C9-H4 = 6.5 [d]	C9-H5 = 7.0
C-10	C10-H3 = 8.0 [d]	C10-H3 = 8.0 [d]	[c]	[c]	[c]	[c]
C-4'	C4'-H5' = 13.5 C4'-4'Me = 7.0	C4'-H4' = 179.0 C4'-5'Me = 4.0	C4'-4'Me = 7.0 C4'-5'Me = 4.0	C4'-H4' = 179.0 C4'-5'Me = 4.0	C4'-H4' = 179.0 C4'-5'Me = 4.0	C4'-4'Me = 7.0 C4'-5'Me = 4.0
C-5'	C5'-H5' = 201.0 C5'-4'Me = 6.5	C5'-H4' = 10.0 C5'-5'Me = 7.0	C5'-4'Me = 6.5 C5'-5'Me = 7.0	C5'-H4' = 10.0 C5'-5'Me = 7.0	C5'-H4' = 10.0 C5'-5'Me = 7.0	C5'-4'Me = 6.5 C5'-5'Me = 7.0
4-Me				C-H = 128.0 4Me-H3 = 5.5		C-H = 128.0 4Me-H3 = 5.5
5-Me					C-H = 127.0	
6-Me	C-H = 128.0 6Me-H5 = 5.0	C-H = 128.0 6Me-H5 = 5.0		C-H = 128.0 6Me-H5 = 5.0	C-H = 128.0	
4'-Me	C-H = 129.0 4'Me-H5' = 1.5		C-H = 128.5			C-H = 128.5
5'-Me		C-H = 129.0 5'Me-H4' = 1.0	C-H = 128.5	C-H = 129.0	C-H = 129.0 5'Me-H4' = 1.0	CH = 128.5

[a] The numbers indicate the position of Me substituents in the angelicin nucleus. [b] Signals not well resolved from noise. [c] Complex multiplet, structure not analyzed. [d] Broadened signals indicating the presence of unresolved coupling(s). [e] Overlapped by other signals. [f] Unassigned coupling.

C-4 *peri* carbons respectively about 3 ppm upfield.

The carbonyl carbon C-2 shows at the lowest field position a readily distinguishable sharp line absorption; this signal is perturbed by the H-3 and H-4 protons, when they are present, with coupling constants of *ca.* 4 and 11 Hz, respectively [13]. The chemical shift range within which its signal falls for the various methylangelicins is quite precisely defined (1.0 ppm), except, as before mentioned, in the case of angelicins carrying a 3-methyl group where absorption moves slightly to low field (1.5 ppm) and shows a quartet splitting of 4.5 Hz.

Of the remaining four quaternary signals (C-7, C-8, C-9 and C-10) the C-7 and C-9 carbons can be localized at lower field position in comparison with the C-8 and C-10 absorption, because of their direct linkage to an oxygen atom [6]. The multiplicity expected and observed for these carbons allows an unequivocal assignment in the proton coupled spectra of angelicin derivatives carrying methyl groups in various positions (Table 3).

The C-9 signal is perturbed by the H-4 and H-5 protons

showing the  $^3J$  C9-H4 and  $^3J$  C9-H5 couplings, respectively 6-7 Hz and 7.5-9 Hz large; these couplings are lacking when the 4 or 5 positions are methylated; no three-bond coupling was observed between C-9 and H4'. The C-7 absorption shows  $^3J$  C7-H5 and  $^3J$  C7-H5' couplings, 9.5-10 Hz and 8 Hz respectively; this absorption however is frequently overlapped by other signals and only in few cases can it be safely analyzed.

For the C-8 signal the following couplings can be assigned  $^3J$  C8-H6 = 4 Hz,  $^3J$  C8-H5' = 6.5 Hz and  $^2J$  C8-H4' = 4-4.5 Hz; the fact that the *para* C8-H6 coupling occurs across an oxygen bonded carbon accounts for its low magnitude [14]. No three-bond C8-4'Me coupling was observed.

The C-10 carbon is perturbed by the H-3 and H-6 protons,  $^3J$  C10-H3 = 8.0 Hz and  $^3J$  C10-H6 = 7.0 Hz; signals, however, are broadening, indicating the presence of other unresolved couplings, probably due to the presence of H-4 and H-5 protons. In addition, when methyl groups are present at the 4 or 5 positions the C-10 absorp-

tion appears as a very complex multiplet.

Moreover, it is noteworthy that the C-7 and C-10 chemical shifts move within a narrow range, 1.9 and 2.5 ppm respectively, while those referring to C-8 and C-9 carbons move significantly, 4.3 and 5.1 ppm respectively; therefore the substituent chemical shift due to the presence of 5 or 6 *para* positioned methyl groups become significant in the last cases, together with the presence of methyl substituents in the pyron or furan ring respectively.

Generally the differences (Table 2) between the substituent chemical shift values predicted for di- and trisubstituted angelicins by a combination of data from monomethylangelicins and those observed are in most cases lower than or equal to 0.4 ppm. However, it can be observed that when two methyl groups are present in a vicinal position, such as in the angelicins carrying methyl groups in the 3,4 or 5,6 or 4',5' positions, the differences between predicted and observed substituent chemical shift values for the carrier carbons are of relevant magnitude and it has been suggested that this fact was due to an *ortho* steric effect [15]. In addition, significative differences for the *peri* C-5 and C-4 carbons in the 3,4 and 5,6 dimethylated angelicins respectively and for C-7 and C-8 carbons in the angelicins dimethylated at the furan ring level or carrying a 5-Me group can also be observed.

The one-bond C-H coupling shows quite significant differences depending on the positions of the carbon atoms. In the angelicins not carrying methyl groups in the pyron ring, the C3-H3 and C4-H4 interactions are quite steady at 172 and 162 Hz respectively. The influence of the introduction of a methyl group into the pyron ring is quite different for these couplings, in fact in the 4-methylangelicins the C3-H3 interaction drops quite consistently by *ca.* 3 Hz, while in the 3-methylangelicins the C4-H4 coupling shows only a negligible lowering (*ca.* 1 Hz) and a lowering of similar magnitude also occurs when a methyl group is present in the *peri* 5 position.

The benzenoid ring one-bond C5-H5 and C6-H6 interactions are equally quite steady at 163 and 167 Hz respectively; they both drop by *ca.* 2 Hz when a methyl group is present in the *ortho* position. The C5-H5 coupling however drops significantly by *ca.* 4 Hz when two methyl groups are contemporaneously present on both the *ortho* 6 and the *peri* 4 position.

As previously observed in psoralen derivatives [4] the largest one-bond couplings are present in the furan ring, 181 and 204 Hz for C4'-H4' and C5'-H5' respectively; they both drop *ca.* 3 Hz when a methyl group is present in the vicinal position.

Two-bond C-H coupling is well observable in the furan moiety,  ${}^2J$  C4'-H5' = 13.5 Hz and  ${}^2J$  C5'-H4' = *ca.* 10 Hz. This interaction is of minor magnitude in the case of C-2 and C-8,  ${}^2J$  C2-H3 = *ca.* 4 Hz and  ${}^2J$  C8-H4' = *ca.* 4 Hz re-

spectively; it was also observed in a few other cases but generally does not apparently seem to be present at measurable magnitude. In addition to those before mentioned for C-2, C-7, C-8, C-9 and C-10 carbons, three-bond inter-ring couplings from C-4 to H-5 and C-5 to H-4 with a magnitude of about 5 Hz are also characteristically seen on those carbon signals.

The substituent methyl groups, as already reported for methylcoumarins [16], have chemical shifts which appear to be good indicators of their positions. These signals in the proton coupled spectra appear as quartets with a constant of about 128 Hz, further splitted by the *ortho* protons with constants of *ca.* 5 Hz for the methyl group linked to the benzene or pyron ring and of *ca.* 1.5 Hz for those linked to the furan ring. In addition, it can be observed that the chemical shifts of two adjacent methyl groups drop characteristically by *ca.* 4-5 ppm except the 4'-Me whose absorption remains unchanged.

## EXPERIMENTAL

Spectra were determined at 20 MHz with a Varian FT-80A spectrometer with 16 K data table for acquisition of free induction decays and by using 10 mm spinning tubes. Saturated solutions of the samples in deuteriochloroform were prepared in order to minimize spectral accumulation times and TMS was added as an internal standard; concentration effects, however, appeared to be of little importance.

Gated decoupling experiments which permitted the retention of nuclear Overhauser enhancement were performed for measurements on carbon-proton coupling constants. Couplings are quoted to the nearest 0.5 Hz and chemical shifts, relative to TMS, to the nearest 0.1 ppm.

All methylangelicins were previously prepared in this laboratory as described elsewhere [10,12,17,18,19,20]. Angelicin was prepared starting from 8-allylumbelliferon [21]; this compound by ozonization and reduction gave the 8-(7-hydroxycoumarinyl)acetaldehyde which by cyclization with concentrated phosphoric acid furnished the desired product, mp 139° (138° [22], 140° [23]).

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