MAGNETIC RESONANCE IN CHEMISTRY, VOL. 27, 348–354 (1989)

^{13}C NMR Spectral Studies of Some Methoxycoumarin Derivatives. A Re-assignment for Citropten (Limettin) and an Examination of *Peri*-Proximity Effects for the Methyl–Methoxy and Methoxy–Methyl Couples

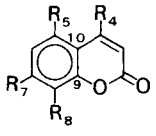
Alan G. Osborne
Department of Chemistry, City University, Northampton Square, London EC1V 0HB, UK

The ^{13}C chemical shifts and ^{13}C–^{1}H coupling constants of some methoxycoumarins are reported. Some earlier spectral assignments, including those for citropten (limettin), require revision. Methoxy substituent effects on long-range ^{13}C–^{1}H couplings in coumarins are highlighted. *Peri*-proximity effects for the methyl–methoxy and methoxy–methyl couples are derived, and the value of these effects in the assignment of *peri*-substituted compounds is illustrated.

KEY WORDS ^{13}C NMR Methoxycoumarins Citropten Limettin ^{13}C–^{1}H coupling constants *Peri*-proximity effects

INTRODUCTION

Although ^{13}C NMR spectral studies of methoxycoumarins have already attracted considerable interest,[1–9] this study indicates that many of the original assignments,[2,3,6] some of which have been perpetuated in more recent work,[8,9] are in need of correction. Amongst the assignments that require significant revision[3,6] are those of the natural product citropten (limettin) (**5**).



	R_4	R_5	R_7	R_8
1	H	H	H	H
2	H	MeO	H	H
3	H	H	MeO	H
4	H	H	H	MeO
5	H	MeO	MeO	H
6	H	MeO	H	MeO
7	Me	H	MeO	H
8	Me	H	Me	H
9	Me	MeO	MeO	H
10	Me	EtO	EtO	H
11	Me	MeO	Me	H
12	MeO	H	MeO	H
13	MeO	Me	MeO	H
14	MeO	Me	H	MeO
15	MeO	H	H	H
16	Me	OH	OH	H

The mis-assignments were first highlighted through a need to identify **2** as a minor product from the Pechmann reaction[10] with *m*-methoxyphenol, as part of our studies on the orientation effects in this synthesis.[7] Duplicate calculations of the estimated chemical shifts for **2** from previous data[3] (see Table 1) were more inconsistent than could be attributed to instrumental error alone.

Table 1. Estimated ^{13}C chemical shifts (δ, ppm) for 2

Carbon	A[a]	B[a]	Difference (A – B)
2	159.4	155.7	+3.7
3	117.8	107.3	+10.5
4	137.8	137.8	0.0
5	158.0	159.6	−1.6
6	103.7	106.1	−2.4
7	129.4	132.2	−2.8
8	110.8	108.7	+2.1
9	154.0	154.9	−0.9
10	109.6	117.2	−7.6

[a] Calculations: *A* = **5** – 7-MeO SCS (**3** – **1**); *B* = **6** – 8-MeO SCS (**4** – **1**).

In this work the ^{13}C NMR chemical shifts of some methoxycoumarins have been carefully assigned from their proton coupled spectra and also through consideration of *peri*-proximity effects where appropriate.

RESULTS AND DISCUSSION

The ^{13}C chemical shifts are reported in Table 2 and ^{13}C–^{1}H coupling constants in Table 3.

Methoxycoumarins

The proton coupled ^{13}C NMR spectra of **4** were very complex and exhibited considerable second-order char-

0749–1581/89/040348–07 $05.00

Received 24 September 1988
Accepted 1 December 1988

Table 2. ^{13}C chemical shifts (δ, ppm) of methoxycoumarins in $CDCl_3$

Carbon	1	2[a]	3	4	4[b]	5	5[b]	7	8[c]	9	10	11
2	160.68	161.13	161.42	160.56	160.27	161.78	160.60	161.62	161.37	161.33	161.46	161.30
3	116.44	114.62	113.16	117.23	116.61	111.04	110.79	112.22	114.21	111.53	111.41	113.56
4	143.67	138.79	143.79	143.96	144.81	139.00	138.95	152.83	152.71	154.74	154.90	154.54
5	128.04	156.49	129.11	119.63	119.87	157.30	157.06	125.77	124.51	159.46	158.73	158.24
6	124.42	105.43	112.67	124.59	124.79	94.93	95.09	112.51	125.61	95.54	96.35	107.54
7	131.79	132.65	163.16	114.13	114.42	164.06	163.94	163.04	143.18	163.12	162.47	143.35
8	116.57	109.25	101.07	147.66	146.93	93.06	93.30	101.07	117.43	93.63	93.95	110.39
9	153.96	155.40	156.16	144.16	143.27	157.10	156.58	155.68	153.93	157.27	157.27	155.60
10	118.81	109.78	112.67	119.79	119.63	104.17	103.31	113.85	117.84	105.06	104.90	108.48
4								18.68	18.60	24.17	24.37	24.29
5		56.11				56.07	56.40			55.78	[d]	55.87
7			55.87			55.91	56.07	55.87	21.61	55.78	[d]	22.01
8				56.44	56.23							

[a] In admixture with **3**.
[b] In DMSO-d_6 solution.
[c] Data from Ref. 7.
[d] CH_3, 14.61; OCH_2, 64.74.

acter owing to the very minimal separation between the H-5, H-6 and H-7 resonances. Indeed, at low field these protons are essentially isochronous;[11] at 360 MHz in DMSO-d_6 solution they still form a closely coupled ABC system, but in $CDCl_3$ solution a perturbed first-order spectrum results. As a consequence, those carbons exhibiting long-range couplings to H-5/H-6/H-7 gave rise to complex ^{13}C multiplets in both solvents, which have not been analysed in this work. Accordingly, assignments were verified by specific proton spin decoupling experiments which confirmed the suggestion of Duddeck and Kaiser[1] that the original assignments[3] of C-3 and C-7 required reversal.

The assignments for **3** were in accordance with earlier work;[3,4] however, the tentative allocations for C-3 and C-6 given by Lapper,[2] which were subsequently employed by Patra[8] as models, should be interchanged. The spectrum of **2**, which has not been reported previously, was examined as the minor component (8%) in admixture with **3** (92%) from the Pechmann reaction[10] with *m*-methoxyphenol. The chemical shifts correlated well with the estimated spectrum [**5** − 7-MeO substituent chemical shift (SCS)], the errors all being below 0.7 ppm, except for C-6 between the methoxy groups (1.25 ppm). The assignments were supported by specific decouplings at H-6 and H-8. Since **2** was only the minor component, it was not possible to determine couplings at the quaternary carbons as the signals were too weak. For the methine carbons J(75) and J(45) were absent, as expected.

Citropten

Examination of the proton coupled spectra of citropten (**5**) indicated that the earlier assignments[3,6] for C-2/C-5 and C-3/C-10 require to be interchanged. In $CDCl_3$ solution the signal for C-3 was a widely spaced simple doublet [J(33)] whereas the quaternary C-10 bridgehead carbon signal was a doublet of triplets. The ^3J couplings to H-3 and H-8 were similar to those reported[5] for **1** whereas J(10, 6), since it occurred across the methoxy substituent, was reduced from 8.5 to 4.9 Hz. In the proton coupled spectrum the two lowest field quaternary carbons absorbed as a doublet of doublets (C-2) and a triplet of quartets (C-7). The enhanced ^2J couplings at C-7 appear to be characteristic of *ipso*-carbons in *meta*-dioxygen substituted systems, as previously noted by Chang *et al.*[5] The C-5/C-9 signals were overlapped in $CDCl_3$, but better resolved in DMSO-d_6 solution as a sextet (C-5) and a doublet of doublets (C-9). At C-5 the couplings (3.7 Hz) can be rationalized as a quartet splitting to OCH_3 [cf. J(7, OMe) 4 Hz],[4] a ^3J(54) doublet and an enhanced ^2J(56) interaction [for **1** J(56) 1.3 Hz)][5] of an *ipso*-carbon in a *meta*-dioxygen substituted system. At C-9, since positions 5 and 7 are occupied, there is a single ^3J interaction to H-4, and also an enhanced ^2J coupling to H-8 which is characteristic of a carbon *ortho* to a *meta*-dioxygen substituted system; thus ^2J(12) of resorcinol (4.1 Hz) is greater than that of phenol (2.5 Hz).[5] The assignments were confirmed by a methoxy spin 'tickled' experiment[12] which collapsed C-7 and C-5 to triplets, but left C-2 and C-9 unaffected. The closely spaced C-6/C-8 peaks were initially assigned by specific proton decouplings at H-6/H-8, which confirmed the earlier tentative results.[3] Moreover, Hansen[13] has noted that in naphthalene derivatives, ^3J couplings that involve β-carbons are generally stronger than those at α-carbons, *viz.* J(24) > J(13). That this relationship is applicable to the carboyclic ring of methoxycoumarins was verified by the proton coupled spectrum of **7**, where assignments of C-6 and C-8 are trivial. It is seen that J(68) > J(86), with both couplings reduced compared with **1** since they occur across the methoxy substituent. Similar couplings apply at C-6 and C-8 in **5**, which supports the assignment. The chemical shift of the carbonyl carbon of **5** is therefore unremarkable, and hence the unusual 2.7 ppm upfield shift noted by Günther *et al.*[3] should be disregarded.

Duplicate calculations of 5-methoxy SCS effects (see Table 4) have differences generally below 0.7 ppm with the largest effect (1.25 ppm) at C-6, *ortho* to the methoxy substituent, which support the present assignments. By addition of the 5-MeO SCS effect to the chemical shifts of **4**, estimated chemical shifts for **6** were

Table 3. ^{13}C–^{1}H coupling constants (Hz) of some methoxycoumarins in $CDCl_3$

Carbon	Coupling	2	5	5[a]	7	9	10	11
C-2		[b]	dd	dd	d	d	d	d
	J(23)		4.7	5.1	4.3	4.3	4.3	4.3
	J(24)		11.7	11.5				
C-3		d	d	d	dq	dq	dq	dq
	J(33)	172.0	172.1	172.7	169.7	175.7	169.0	169.0
	J(3, Me)				5.5	6.1	6.1	6.1
C-4		d	d	d	m[c]	q	q	q
	J(44)	166.0	163.2	165.0				
	J(4, Me)					6.1	6.1	6.1
C-5		[b]	sext.	sext.	d	quin.	m	m
	J(55)				161.7			
	J(54)		3.9	3.7				
	J(56)		3.9	3.7		3.9		
	J(5, OMe)		3.9	3.7		3.9		
C-6		dd	dd	dd	dd	dd	dd	ddq
	J(66)	162.3	161.1	162.4	163.4	160.6	160.2	158.7
	J(68)	7.3	4.9	4.9	4.9	4.9	4.9	6.7
	J(6, Me)							4.9
C-7		d	tq	sext.	m	sext.	m	q
	J(77)	158.7						
	J(76)		4.4	3.8		4.3		
	J(78)		4.4	3.8		4.3		
	J(7, OMe)		3.2	3.8		4.3		6.1[d]
C-8		dd	dd	dd	dd	dd	dd	dquin.
	J(88)	167.2	164.8	166.0	164.2	164.8	164.8	164.2
	J(86)	7.3	4.3	4.3	4.3	4.3	4.3	5.5
	J(8, Me)							5.5
C-9		[b]	dd	dd	m	d	d	d
	J(94)		6.1	6.0				
	J(98)		4.9	5.0		4.9	4.9	3.0
C-10		[b]	dt	dt	m	m	m	m
	J(10, 3)		8.6	7.9				
	J(10, 6)		4.9	5.5				
	J(10, 8)		4.9	5.5				
4-Me					qd	qd	qd	qd
	J(Me)				128.2	130.0	129.4	129.4
	J(Me, 3)				5.5	6.1	6.1	6.1
5-OMe		q	q	q		q	tq[e]	q
	J(MeO)	144.6	145.3	145.9		144.6	144.0	144.6
7-OMe			q	q	q	q	tq[e]	
	J(MeO)		144.7	145.3	144.7	144.6	144.0	
7-Me								qt
	J(Me)							127.0
	J(Me, 6)							4.3
	J(Me, 8)						[f]	4.3

[a] In DMSO-d_6.
[b] Peak not visible, intensity too small.
[c] m = multiplet (not analysed).
[d] J(7, Me).
[e] OCH_2, $^2J(OCH_2, CH_3)$ 4.3 Hz.
[f] $\underline{C}H_3CH_2$, J(Me) 127.0 Hz.

obtained, which supported the earlier assignments.[3] The calculations were not sufficiently precise to distinguish between the closely separated C-3 and C-7; however, the coupled spectrum would facilitate identification.

Peri-substituted coumarins

Parmar *et al.*[9] recently reported a ^{13}C NMR spectral study of 36 4-methylcoumarin derivatives, which

Table 4. Revised 5-methoxy substituent chemical shift calculations (ppm)

Carbon	A^a	B^a	Difference $(A-B)$
2	+0.45	+0.36	+0.09
3	−1.82	−2.12	+0.30
4	−4.88	−4.79	−0.09
5	+28.45	+28.19	+0.26
6	−18.99	−17.74	−1.25
7	+0.86	+0.90	−0.04
8	−7.32	−8.01	+0.69
9	+1.44	+0.94	+0.50
10	−9.03	−8.50	−0.53

[a] Calculations: $A = \mathbf{2} - \mathbf{1}$ (see Table 2), values used for calculation of Me–MeO *peri*-couple; $B = \mathbf{5} - \mathbf{3}$ (see Table 2).

included **7**. Since their assignments were based on SCS effects alone, it would now appear that the closely spaced C-3 and C-6 signals were mis-assigned. In the coupled spectrum the upfield signal exhibits a fine quartet splitting [J(3, Me)], indicating that it must be due to C-3. Their study also featured several *peri*-substituted compounds including **9**. It would appear, however, that the effect of the Me–MeO couple was not considered, and consequently the assignments for all six quaternary carbons are in need of revision. (The following nomenclature is suggested with respect to *peri*-couples with different substituents: the order of substituents in the couple is the same as the order of ring substituent numbering. Hence 4-methyl-5-methoxy- is a methyl–methoxy couple and 4-methoxy-5-methyl- is a methoxy–methyl couple.) In the coupled spectrum (see Fig. 1) the five well separated low-field quaternary signals appear as a sextet (C-7), doublet (C-2), quintet (C-5), doublet (C-9) and quartet (C-4). The assignments were supported by a series of spin 'tickled' experiments[12] at H-3, CH_3 and H-8 which collapsed C-2, C-4 and C-9, respectively, to singlets, whereas when the methoxy resonances were tickled the C-7 signal became a triplet and that of C-5 a doublet (see Fig. 1), these being enhanced ^2J couplings of *ipso*-carbons in a *meta*-dioxygen substituted system. The peak allocations were also in accordance with their intensities; C-4, bonded to methyl, had the highest intensity signal with the expected shortest relaxation time, whereas C-2/C-9, each with only one hydrogen two bonds distant, were lowest. The methoxy-substituted carbons were intermediate, with C-7 (two adjacent *ortho*-hydrogens) larger than C-5 (one adjacent *ortho*-hydrogen). Parmar *et al.*[9] reported that the C-10 signal was overlapped with that of C-3 at δ 111.14, whereas in this work it absorbed at δ 105.06. It was, however, a very low-intensity signal, but with both positions 4 and 5 occupied a long T_1 would be expected. Differentiation between the closely spaced C-6/C-8 resonances was again achieved through specific decouplings and application of the $J(68) > J(86)$ rule as used for **5** and **7**. The spectrum of **10** was very similar, which implied that the Me–MeO and Me–EtO *peri*-proximity effects appeared to be mainly dependent on the nature of the key atom, i.e. oxygen. Another *peri*-substituted

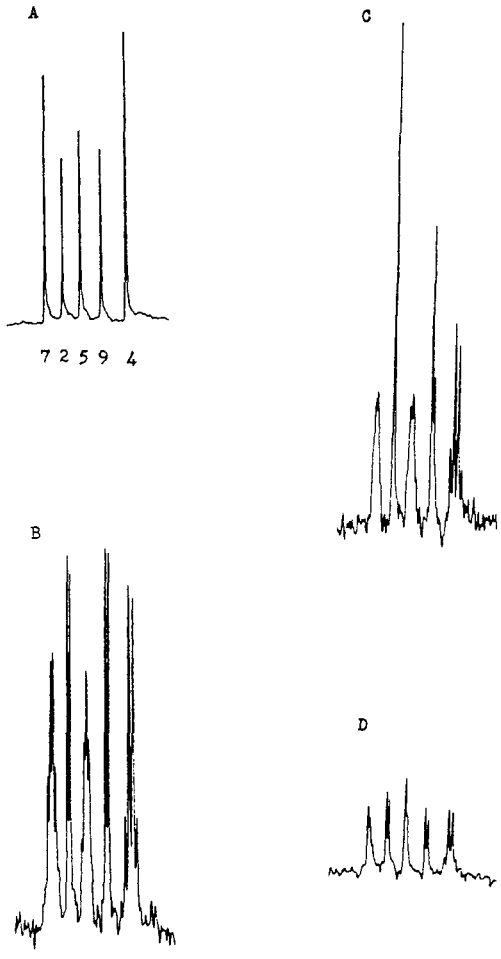


Figure 1. ^{13}C NMR spectra of **9** (δ 150–165 ppm region). (A) Proton decoupled; (B) proton coupled; (C) H-3 spin 'tickled'; (D) OCH_3 groups spin 'tickled'.

compound containing the Me–MeO couple, **11**, has also been examined. The assignments were made from the coupled spectrum as in the case of **9**. As expected no J(76) or J(78) couplings were present for the 7-methyl compound, and again $J(68) > J(86)$, but the couplings were less reduced across the methyl group.

The *peri*-proximity effect represents the deviation[14] between experimental and estimated chemical shifts ($\delta_{expt.} - \delta_{est.}$). For **9** the estimated chemical shifts were obtained from **7** + 5-MeO SCS (see Table 4) and from **5** + 4-Me SCS,[15] and for **11** from **8** + 5-MeO SCS. The *peri*-proximity effects for **9** and **11** were then calculated (see Table 5) and compared. They represent a measure of the degree of molecular distortion introduced in order to relieve the repulsive interaction between the *peri*-substituents.[16] The effects were generally very similar with the best correlations at C-4, C-5, CH_3 and OCH_3, closest to the site of *peri*-substitution. From the work of Lapper[2] upon the *peri*-substituted natural product siderin (**13**), the *peri*-proximity effect for the MeO–Me couple was determined (see Table 6). The estimated chemical shifts were obtained from **12** + 5-Me SCS.[15] Comparison of the Me–MeO and MeO–Me couples (see Fig. 2) indicates that characteristic effects of each particular substituent appear to be manifested in each ring system. As previously experienced for the

Table 5. Calculation of *peri*-proximity effects (ppm) for the Me–MeO couple in coumarins

Carbon	**9** *A*[a]	**9** *B*[a]	**11** *C*[a]
C-2	−0.74	−0.35	−0.52
C-3	+1.13	+2.09	+1.17
C-4	+6.79	+6.84	+6.71
C-5	+5.24	+5.46	+5.28
C-6	+2.02	+0.81	+0.92
C-7	−0.78	−0.84	−0.69
C-8	−0.12	+0.37	+0.28
C-9	+0.15	+0.77	+0.23
C-10	+0.24	−0.21	−0.33
4-Me	+5.49	+5.49	+5.69
5-MeO	−0.33	−0.33	−0.24

[a] Calculations: *A* = **9** (expt.) − **9** (est.) from **7** + 5-MeO SCS (Table 4); *B* = **9** (expt.) − **9** (est.) from **5** + 4-Me SCS (Ref. 15); *C* = **11** (expt.) − **11** (est.) from **8** + 5-MeO SCS (Table 4).

Table 6. Calculation of *peri*-proximity effects (ppm) for the MeO–Me couple in coumarins

Carbon	13 chemical shifts Est. (*A*)[a]	Expt. (*B*)[a]	MeO–Me *peri*-effect (*C*)[a]
C-2	162.6	162.7[b]	+0.1
C-3	86.5	87.4	+0.9
C-4	163.2	169.3	+6.1
C-5	131.9	138.2	+6.3
C-6	112.9	115.4	+2.5
C-7	162.4	161.6[b]	−0.8
C-8	98.0	98.6	+0.6
C-9	155.0	156.3	+1.3
C-10	107.3	107.6	+0.3
4-MeO	56.1	55.8	−0.3
5-Me	18.2	23.4	+5.2

[a] Calculations; *A* = **12** (Ref. 2) + 5-Me SCS (Ref. 15); *B* = data from Ref. 2; *C* = *B* − *A*.
[b] Tentative assignment.

Me–Me couple in naphthalene[14] the effects at the *ipso*-carbons are positive, with *ipso*-CH_3 > *ipso*-OCH_3 in each type of couple. At positions 3 and 6 (*ortho* to the *peri*-substituents), positive effects again occur, with CH_3 producing the larger effect; at the *meta*-positions the effects are generally negative. For C-10, between the *peri*-substituents, the effect is small and of variable sign. Accordingly, these general trends, many of which are of considerable magnitude, must be considered during the assignment of *peri*-substituted compounds, otherwise significant errors, as reported[9] for **9**, may result. The assignments for the other *peri*-substituted compounds

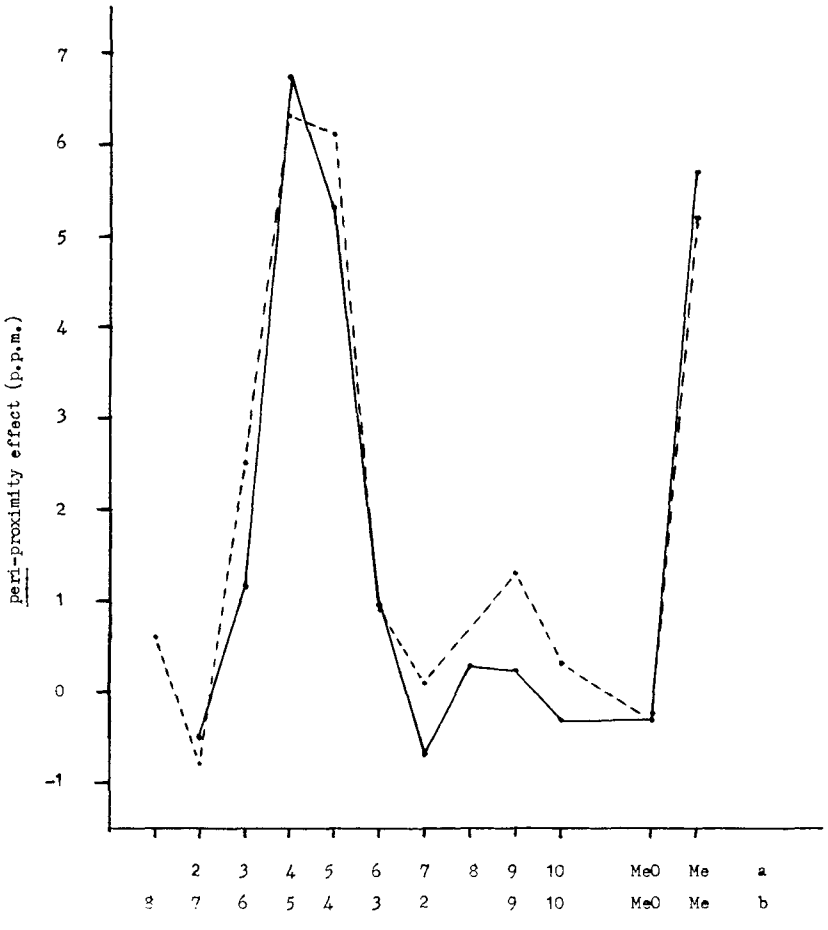


Figure 2. Comparison of *peri*-proximity effects for (a) the Me–MeO couple (solid line) and (b) the MeO–Me couple (broken line).

studied by Parmar *et al.*[9] should therefore be viewed with caution.

Some comments on other studies of the ^{13}C NMR spectra of methoxycoumarin derivatives are now appropriate.

Grigor and Webb[17] calculated nuclear screening tensors for methoxycoumarins and plotted the results against the chemical shifts reported by Günther *et al.*[3] Revised presentation of these data using the amended chemical shift assignments obtained here was found to give an improved correlation, particularly for C-3 and C-10 of **5**.

Bangov[18] reported an approach for the automatic assignment of ^{13}C NMR spectra based on a chemical shift–charge density relationship. The correlation obtained for **3** was eventually regarded as satisfactory 'to ensure the correct assignment in this particular case.' This result is indeed exceptional since, in error, the chemical shift data[3] used for the correlation was that of the mis-assigned **4** and not **3**, with the chemical shift differences at C-7 and C-8 amounting to no less than 45.8 and 46.5 ppm, respectively!

Joseph-Nathan *et al.*[19] isolated a new coumarin, named 8-methoxypereflorin (**14**), from *Perezia multiflora*. The CH_3 group absorbed at δ 22.7, a 4.5 ppm downfield shift from 5-methylcoumarin;[15] this is clearly characteristic of a MeO–Me *peri*-couple and would have located the methyl substituent immediately. However, the claim that the estimated chemical shifts were 'in reasonable agreement' would appear to be unjustified since the proximity effect does not appear to have been considered. A revised estimation (see Table 7) from **15**[4] + 8-MeO SCS (Table 2) + 5-Me SCS[15] + MeO–Me *peri*-proximity effect (Table 6), however, is in excellent agreement. The larger errors at C-5 (−1.29 ppm) and C-6 (−1.47 ppm) probably arise from the need to employ results from five different laboratories in the compilation. The above example clearly illustrates that, for the unambiguous assignment of *peri*-substituted coumarins, a contribution from the relevant proximity effect couple must be included in any estimation of chemical shifts.

Table 7. Estimated ^{13}C chemical shifts (δ, ppm) for 14

Carbon	14 chemical shifts Est. (*A*)[a]	Expt. (*B*)[a]	Difference (*B* − *A*)
C-2	161.68	161.8	+0.12
C-3	90.89	90.2	−0.69
C-4	169.19	169.2	+0.01
C-5	128.79	127.5	−1.29
C-6	127.87	126.4	−1.47
C-7	113.84	113.5	−0.34
C-8	145.89	145.7	−0.19
C-9	144.70	144.5	−0.20
C-10	115.18	114.9	−0.28
4-MeO	56.5	56.3	−0.20
8-MeO	56.44	55.9	−0.54
5-Me	23.4	22.7	−0.70

[a] Calculations: *A* = **15** (Ref. 4) + 8-MeO SCS (from Table 2) + 5-Me SCS (Ref. 15) + MeO–Me *peri*-proximity effect (Table 6); *B* = data from Ref. 19.

EXPERIMENTAL

Compounds

Compounds **1** and **5** were commercial samples. Compounds **7** (m.p. 158–159 °C, lit.[20] m.p. 158–159 °C), **8** (m.p. 131–132 °C, lit.[7] m.p. 131–132 °C), **9** (m.p. 173–174 °C, lit.[21] m.p. 171 °C) and **11** (m.p. 147–148 °C, lit.[22] m.p. 147 °C) were prepared by established methods. Compound **4** (m.p. 88–89 °C, lit.[23] m.p. 88 °C) was synthesized by the technique of Mauthner[23] using potassium acetate in place of sodium actate. ^{1}H NMR (360 MHz, $CDCl_3$): 3.909 (3H, s, OCH_3); 6.376 [1H, d, *J*(34) 9.5 Hz, H-3]; 7.012 [1H, dd, *J*(56) 7.7 Hz, *J*(57) 1.4 Hz, H-5]; 7.037 [1H, dd, *J*(67) 8.1 Hz, *J*(57) 1.4 Hz, H-7]; 7.157 [1H, dd, *J*(56) 7.7 Hz, *J*(67) 8.1 Hz, H-6]; 7.653 [1H, d, *J*(34) 9.5 Hz, H-4]. ^{1}H NMR (360 MHz, DMSO-d_6): 3.899 (3H, s, OCH_3); 6.483 [1H, d, *J*(34) 9.5 Hz, H-3]; 7.245, 7.263, 7.280 (1H, 1H, 1H, ABC system, H-5, H-6, H-7, respectively); 8.020 [1H, d, *J*(34) 9.5 Hz, H-4].

Pechmann reaction of *m*-methoxyphenol and malic acid in concentrated sulphuric acid at 120–130 °C, under conditions reported previously,[7] gave a crude orange product which was a mixture of **3** (92%) and **2** (8%). Extraction of the crude product with boiling light petroleum (b.p. 60–80 °C) afforded a purer sample as colourless plates with the same methoxycoumarin isomer ratio. ^{1}H NMR (360 MHz, $CDCl_3$) (peaks for **2** only): 3.888 (3H, s, OCH_3); 6.279 [1H, d, *J*(34) 9.8 Hz, H-3]; 6.673 [1H, broadened d, *J*(67) 8.4 Hz, H-6]; 6.853 [1H, ddd, *J*(78) 8.4 Hz, *J*(68) 1.4 Hz, *J*(48) 0.6 Hz, H-8]; 7.392 [1H, t, *J*(67) ≈ *J*(78) 8.4 Hz, H-7); 8.036 [1H, dd, *J*(34) 9.8 Hz, *J*(48) 0.6 Hz, H-4].

A mixture of **16**[21] (2.7 g), ethyl iodide (26 ml) and potassium carbonate (10 g) in acetone (100 ml) was boiled under reflux for 48 h. After removal of the solvent by distillation, water (100 ml) was added and the product collected by filtration. Compound **10** (2.8 g, 84%) crystallized from methanol as colourless needles, m.p. 152–153 °C. Found, C 67.70, H 6.58; calculated for $C_{14}H_{16}O_4$, C 67.73, H 6.50%. ^{1}H NMR (100 MHz, $CDCl_3$): 1.48/1.52 (each 3H, t, *J* 7 Hz, 2 × $OCH_2\underline{CH_3}$); 2.60 [3H, d, *J*(Me, 3) 1 Hz, CH_3]; 4.13 (4H, q, *J* 7 Hz, 2 × OCH_2); 5.99 [1H, *J*(3, Me), 1 Hz, H-3]; 6.32 [1H, d, *J*(68) 2.5 Hz, H-6]; 6.45 [1H, d, *J*(68) 2.5 Hz, H-8].

NMR spectra

All samples were examined as dilute solutions in $CDCl_3$ (and also in DMSO-d_6 for **4** and **5**) containing TMS as reference; chemical shifts are reported as δ ppm. The ^{13}C–{^{1}H} spectra were recorded at 15 MHz (Jeol FX-60 spectrometer), pulse width 7 μs (45° pulse angle), pulse repetition rate 4 s, spectral width 2500 or 1000 Hz, 8K data points with noise decoupling at 55 dB. For proton coupled spectra, the 'Gated-1' alternatively pulsed sequence was used. For specific proton decouplings the CW power level was 30 dB and for spin 'tickling'

experiments it was 5 dB. ^{1}H NMR spectra were recorded at 100 MHz on a Jeol JNM-MH-100 spectrometer and at 360 MHz on a Bruker WH-360 spectrometer (at the University of Edinburgh).

Acknowledgements

Thanks are due to the SRC (now SERC) for providing funds to purchase the NMR instrumentation and for providing access to the facilities at the University of Edinburgh. Thanks are also due to undergraduate students S. J. Andrews and Ms A. P. L. Tiong for assistance with the synthesis of the compounds.

REFERENCES

1. H. Duddeck and M. Kaiser, *Org. Magn. Reson.* **20**, 55 (1982).
2. R. D. Lapper, *Tetrahedron Lett.* 4293 (1974).
3. H. Günther, J. Prestian and P. Joseph-Nathan, *Org. Magn. Reson.* **7**, 339 (1975).
4. N. J. Cussans and T. N. Huckerby, *Tetrahedron* **31**, 2719 (1975).
5. C.-j. Chang, H. G. Floss and W. Steck, *J. Org. Chem.* **42**, 1337 (1977).
6. K. Jewers and K. A. Zirvi, *Planta Med.* **33**, 403 (1978).
7. A. G. Osborne, *Tetrahedron* **37**, 2021 (1981).
8. A. Patra, *J. Indian Chem. Soc.* **63**, 417 (1986).
9. V. S. Parmar, S. Singh and P. M. Boll, *Magn. Reson. Chem.* **26**, 430 (1988).
10. H. von Pechmann, *Chem. Ber.* **17**, 929 (1884).
11. W. Brügel, *Handbook of NMR Spectral Parameters*, Vol. 1, p. 181. Heyden, London (1979).
12. S. R. Johns, R. I. Willing, P. A. Claret and A. G. Osborne, *Aust. J. Chem.* **32**, 761 (1979).
13. P. E. Hansen, *Org. Magn. Reson.* **12**, 109 (1979).
14. N. K. Wilson and J. B. Stothers, *J. Magn. Reson.* **15**, 31 (1974).
15. L. Ernst, *J. Magn. Reson.* **21**, 241 (1976).
16. P. A. Claret and A. G. Osborne, *Spectrosc. Lett.* **11**, 351 (1978).
17. G. I. Grigor and G. A. Webb, *Org. Magn. Reson.* **9**, 477 (1977).
18. I. P. Bangov, *Org. Magn. Reson.* **16**, 296 (1981).
19. P. Joseph-Nathan, J. Hidalgo and D. Abramo-Bruno, *Phytochemistry* **17**, 583 (1978).
20. J. I. Okogun, V. U. Enyenihi and D. E. U. Ekong, *Tetrahedron* **34**, 1221 (1978).
21. F. W. Canter, F. H. Curd and A. Robertson, *J. Chem. Soc.* 1255 (1931).
22. R. J. Parikh and S. Sethna, *J. Indian Chem. Soc.* **27**, 369 (1950).
23. N. Mauthner, *J. Prakt. Chem.* **152**, 23 (1939).