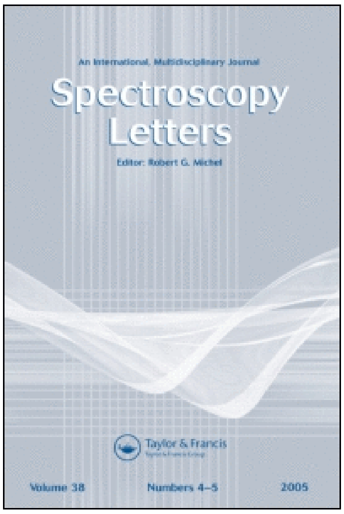

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N.M.R. Spectral Studies of Some Quinolone Derivatives. VIII. ^{13}C-^{1}H Coupling Constants for the 2-Quinolone System

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N.M.R. SPECTRAL STUDIES OF SOME QUINOLONE DERIVATIVES.

Part 8.[1] ^{13}C - ^{1}H COUPLING CONSTANTS FOR THE 2-QUINOLONE SYSTEM

Key Words : long range J_{CH} coupling constants, NMR, 2-quinolone, second order effects

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Abstract : One bond and long range J_{CH} coupling constants for a series of 2-quinolone derivatives are described. The spectra of the parent compound shows considerable second order character at both 15 MHz and 90 MHz in $CDCl_3$ and in DMSO-d_6 solution, which has been discussed. The variations in the coupling patterns resulting from the fusion of the lactam ring and change of heteroatom are highlighted.

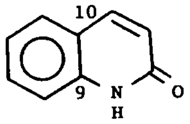
INTRODUCTION

Studies of short and long range ^{13}C - ^{1}H coupling constants have already attracted considerable interest,[2-5] and several rules governing the nature and magnitude of the interactions have now been established.[6-10] However, as far as the present author is aware, no detailed examination of the 2-quinolone system has yet been reported; in this paper a study of ^{13}C - ^{1}H couplings for a series of 2-quinolones (1 - 16) is presented, From related studies of the 2-pyridone (17),[6,9] quinoline(18)[4,7] and coumarin (19)[5,8] ring systems it has been established that the short range ^1J interactions are enhanced when closer to the heteroatom. The most significant long range interactions are the ^3J (meta) couplings. Moreover, in common with earlier studies[11] on naphthalene (20), those carbocyclic ring couplings of 18 that involve β-carbons (6,7) are generally stronger than those at the α-carbons (5,8).[7] Significant ^2J splittings are general only observed[4,8] in heteroaromatics when the carbon or proton involved is ortho to the heteroatom (viz J_{23} or J_{32}). The bridgehead carbon ^3J interactions may be classified as "cross" ring and "through" ring couplings,[12] whilst in 19 an additional $^2J_{98}$ splitting has been reported.[8] Some long range J_{CH} couplings have been presented for the pyranoquinoline alkaloid 8-methoxyflindersine.[13]

The present work involved the extensive use of methyl substituents as "blocking" groups, both ^2J (from ipso-carbon) and ^3J long range alkyl C/H interactions have been reported;[7,17] for the quinoline (18) series.

For our previous studies of the 2-quinolone (1) and 4-quinolone systems a common solvent system of 9:1 DMSO-d_6 : $CDCl_3$ was used.[15] For the present work, in order to avoid any complications from media effects, the appropriate single solvents have instead been employed, however, certain samples then proved too insoluble for examination. Since syntheses commencing from meta-toluidine or 3,4-dimethylaniline, often lead to the 7- or 6,7- isomer being formed either exclusively (e.g. 8)[16] or in greater proportion (e.g. 5,12)[17,28] the number of 5-substituted derivatives available was somewhat limited. No attempt has been made to prepare any 3-substituted 2-quinolones,[18] however, this did not inhibit the analysis of the heteroring interactions.

The proton coupled ^{13}C N.M.R. spectrum of 1 was initially examined at 15 MHz in $CDCl_3$. Second order effects were apparent at C-5



1

4-Me-1	2	4,6-Me_2-1	7	4,5,7-Me_3-1	15
5-Me-1	3	4,7-Me_2-1	8	6-Cl-1	16
6-Me-1	4	4,8-Me_2-1	9		
7-Me-1	5	5,7-Me_2-1	10		
8-Me-1	6	5,8-Me_2-1	11		
		6,7-Me_2-1	12		
		6,8-Me_2-1	13		
		7,8-Me_2-1	14		

and C-6, whilst an unexpected additional splitting was seen at C-7; furthermore the bridgehead carbon signals were unresolved (see Table 1). Since a complete analysis was therefore not possible, the spectrum was also examined in DMSO-d_6 in an attempt to obtain the coupling parameters for the parent compound. However, similar difficulties were again experienced (see Table 1). Consequently, a series of substituted derivatives (2 - 16) was then investigated in $CDCl_3$ solution. These were designed so as to "block" certain interactions such that from the resultant first order systems the remaining couplings could then be resolved (see Table 2).

A later opportunity then became available for a limited high field study. In DMSO-d_6 solution the 360 MHz ^1H N.M.R. spectrum of 1 (see Table 4) was well separated in agreement with an earlier study.[19] However, in $CDCl_3$ solution the chemical shifts of H-5, H-7 and H-8 were very close such that the ABCD system was severely perturbed.

The 90 MHz proton coupled ^{13}C N.M.R. spectrum of 1 in DMSO-d_6 showed first order behaviour for seven of the carbons, however, in

Table 1

^{13}C Chemical shifts (δ) and ^{13}C - ^{1}H coupling constants (Hz) of 2-quinolone (1) at 15 MHz and 90 MHz (a)

Solvent	$CDCl_3$		DMSO-d_6	
	15 MHz	90 MHz	15 MHz	90 MHz
Carbon				
2	 dd 1.5 (3) 10.3 (4)	165.09 dd 1.7 (3) 10.3 (4)	 dd 1.9 (3) 10.3 (4)	161.96 dd 1.9 (3) 10.3 (4)
3	 d 169.7 (3)	121.48 d 163.5 (3)	 d 167.7 (3)	121.93 d 167.7 (3)
4	 dd 162.8 (4) 95.2 (5)	141.38 dd 162.8 (4) 5.2 (5)	 dm 163.3 (4)	140.24 dd 162.2 (4) 5.1 (5)
5	 dm 160.6 (5)	128.00 dm 159.5 (5)	 dm 161.2 (5)	127.88 ddd 161.0 (5) 7.7 (7) 4.0 (4)
6	 dm 171.4 (b)	122.93 dm 170.9 (b)	 dm -	121.76 dm 162.0 (6) 7.9 (8)
7	 ddd 161.4 (7) 8.3 (5) 1.5 (x)	130.93 ddd 160.7 (7) 8.4 (5) 2.0 (x)	 ddd 161.6 (7) 8.5 (5) 1.5 (x)	130.35 ddd 161.4 (7) 8.5 (5) 2.0 (x)
8	 dd 162.8 (8) 7.3 (6)	116.63 dd 162.5 (8) 7.5 (6)	 dd 163.3 (8) 7.1 (6)	115.16 dd 163.2 (8) 7.1 (6)
9	 br "q" _ca_. 7	138.92 br "q" _ca_. 7	 br "q" _ca_. 7	138.92 br "q" _ca_. 7
10	 br "t"	120.27 co "t"	 br "t"	119.13 br "t"

(a) Data for each carbon shown in following order : chemical shift (at 90 MHz only), multiplicity (short range interaction in **bold**) and coupling constants (coupled proton shown in parentheses) : d = doublet, m = multiplet, br = broadened, co = complex, "t"/"q" = triplet/quartet appearance. (x) = frequency dependent "virtual" splitting (see discussion).

(b) $J_{66} + J_{68}$.

$CDCl_3$ second order effects still persisted at C-5, C-6, C-7 and C-10 (see Table 1). These spectral observations are consistent with the known[20,21] inter-relation between second order ^{13}C - ^{1}H coupling effects and the associated complexity of the ^{1}H spectrum. Thus the analysis of the ^{13}C - ^{1}H coupling pattern of 1 appears to be far from trivial.

Coupling constant values obtained at both 15 MHz and 90 MHz are shown in Table 1, Those at high field are considered the more accurate and reliable because of the improved digital resolution employed. For those carbons displaying first order character (e.g. C-2 and C-8) the values at both frequencies are generally very consistent, however, for those carbons where second order effects occur the deviations are sometimes more significant. Results at both frequencies have been included so as to illustrate the limitations of the low field study. In the discussion that follows ring splittings at each carbon are considered initially for the parent 2-quinolone (1), at low and high field in both solvents (see Table 1), supported by the results from the low field study of selected derivatives which were used to confirm the coupling modes and magnitudes (see Table 2). A separate discussion of alkyl proton/carbon interactions then follows, these results are collected in Table 3.

The carbonyl carbon, C-2, consistently appeared as a first order doublet of doublets. That the stronger coupling was to H-4 was confirmed by the clear fine doublet observed for **2** and **8**. The magnitude of J_{24} (10.3 Hz) was more consistent with that observed for the bicyclic **19** (11.5 Hz),[8] than for **17** (6.7 Hz)[9] possibly due to the effects of benzene ring fusion. In contrast, the J_{23} splittings in 1 and **17** were very similar.

The C-3 methine carbon was observed as a **doublet** (short range ^{1}J interactions are shown in **bold**), however, the J_{33} values in $CDCl_3$ were

Table 2

Selected ^{13}C - ^{1}H coupling constants in some 2-quinolone derivatives at 15 MHz (a)

Carbon	Compound(s)	Peak mult. (b)	J (Hz)		
2	2,8	d	J_{23}	1.8	
3	5,6	d	J_{33}	169.6	
	2	dq	J_{33}	166.0	(c)
4	10,11	d	J_{44}	160.0	
	7,8	dq	J_{45}	4.2	(c)
5	8	d	J_{55}	159.4	
	5,14	dd	J_{55}	160.5	
			J_{54}	4.3	
	7	ddq	J_{55}	158.1	
			J_{57}	7.3	(c)
6	2	dm	$J_{66}+J_{68}$	170.9	(d,e)
	6,9	d	J_{66}	162.4	
	13	q	(c)		
7	3	d	J_{77}	160.2	
	10	q	(c)		
	6	ddq	J_{77}	158.7	(c)
	7	ddq	J_{77}	159.4	
			J_{75}	7.3	(c)
	13	ddqq	J_{77}	156.3	
			J_{75}	7.3	(c)
	5,8	dq	J_{75}	7.3	(c)
	2	dd	J_{77}	161.1	
			J_{75}	8.6	(f)
8	4,7	d	J_{88}	161.7	
	13	q	(c)		
	5	ddq	J_{88}	160.0	
			J_{86}	6.1	(c)

Table 2 Continued

Carbon	**Compound(s)**	**Peak mult. (b)**	**J (Hz)**		
	8	ddq	J_{88}	159.3	
			J_{86}	6.2	(c)
	12	dq	J_{88}	159.3	(c)
9	15 (g)	s	-		
	8	d	J_{95}	7.9	
	10	d	J_{94}	4.9	
	3	dd	J_{94}	4.9	
			J_{97}	7.1	
	5	dd	J_{94}	6.1	
			J_{95}	7.3	
	2,7	t	J_{95}-J_{97}	7.3	
	12	dd	J_{94}	4.9	
			J_{95}	6.0	
10	13	d	$J_{10.3}$	8.0	
	4	m	-		
	16	dd	$J_{10.3}$	8.1	
			$J_{10.8}$	6.1	
	7	dd (h)	$J_{10.3}$	5.5	
			$J_{10.8}$	4.9	
	6,14	dd	$J_{10.3}$	8.0	
			$J_{10.6}$	6.2	

(a) Values are quoted only in those instances where the 90 MHz spectral interpretation is either ambiguous or requires additional confirmation.

(b) ^1J interactions shown in **bold**.

(c) For coupling(s) to alkyl protons, see Table 3.

(d) X component of ABX system.

(e) Multiplet splitting pattern similar to 1.

(f) No additional fine splitting present.

(g) In mixed DMSO-d_6, $CDCl_3$, Me_2CO-d_6 solvent.

(h) With methyl couplings selectively decoupled.

Table 3

^{13}C –^{1}H Coupling constants (Hz) in some
alkyl 2-quinolone derivatives at 15 MHz

(A)	**One bond**	**Coupling constant**		**Compound(s)** (a)
	Me-4	128.2		2,7
	Me-5	126.9		3,10
	Me-6	126.4		4,13
	Me-7	126.9		5,8,12,14
	Me-8	126.9		6,9,13
(B)	**^{3}J Methyl C – ring H**		J_{CH}/J_{HH} (b,c)	
	4-Me.3	6.1	0.64	2,7,8,9
	5-Me.6	4.9	0.63	3,10
	6-Me.5	4.9	0.63	12,13
	6-Me.7	4.3	0.63	13
	7-Me.6	4.3	0.63	5,8,14
	7-Me.8	4.9	0.59	5,8,12
	8-Me.7	4.9	0.59	6.9,13
(C)	**Ring C – methyl H**			
(^{2}J)	4-Me.4	6.1		7,8,9
	5-Me.5	obsc.		
	6-Me.6	6.1		4,7,13
	7-Me.7	5.5		5,10
	8-Me.8	6.1		13
(^{3}J)	3-Me.4	5.5	0.58	2,7,9
	5-Me.6	5.5	0.71	7
	6-Me.5	obsc.		
	6-Me.7	4.9	0.72	14
	7-Me.6	4.9	0.72	7,13
	7-Me.8	5.5	0.66	13
	8-Me.7	5.5	0.66	5,8,12

(a) Compound(s) from which coupling quoted was/were taken, other compounds studied gave similar values (± 0.5 Hz).

(b) Proton couplings used (see Table 4) were : J_{34} 9.5 Hz, J_{56} 7.8 Hz, J_{67} 6.8 Hz, J_{78} 8.3 Hz.

(c) See reference 14.

significantly different when measured at different frequencies. Possibly that at 15 MHz was subject to a second order effect, however, similar values close to 169 Hz were obtained for 5,6 and other compounds. J_{33} was reduced when an *ortho*-methyl group was present, as in 2 in contrast the values of J_{33} in DMSO-d_6 were consistent and very similar to that found[6,9] in 17. Ballesteros *et al.*[9] have reported a

Table 4

360 MHz ^1H N.M.R. spectra of 2-quinolone (1)

	$CDCl_3$	$DMSO-d_6$ (a)
Chemical shift (δ)		
H-3	6.719	6.491
H-4	7.807	7.882
H-5	7.549	7.636 (7.771)
H-6	7.202	7.153 (7.286)
H-7	7.500	7.479 (7.609)
H-8	7.455	7.304 (7.474)
Coupling constants (Hz)		
J_{34}	9.5	9.5
J_{56}	7.8	7.8
J_{67}	6.8	7.2
J_{78}	8.3	8.2
J_{57}	1.4	1.4
J_{68}	1.5	1.2
J_{58}	0.7	0.6
J_{48}	0.7	0.6

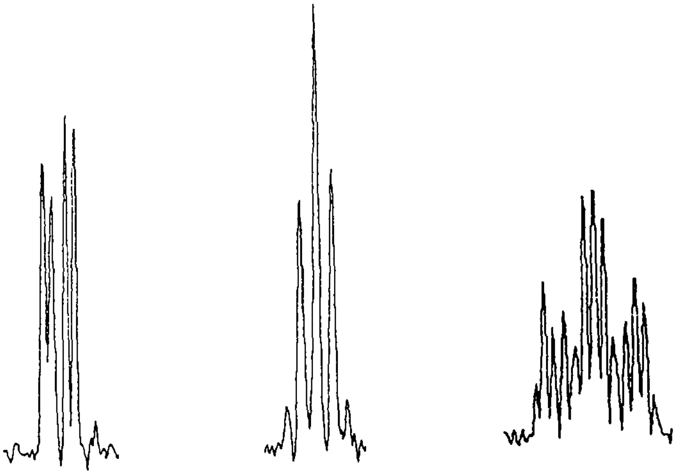
(a) Data from reference 19 (100 MHz) shown in parentheses.

weak J_{34} interaction (1.4 Hz) in **17**, which was not observed in 1, the doublet lines being very sharp.

A well resolved doublet of narrow doublets was generally observed for C-4. Since the long range splitting was absent in both **10** and **11** it may be regarded as the small *peri*-coupling J_{45}, as also seen in the flindersine series.[13] When C-4 was quaternary (*e.g.* **7,8**) the weak *peri*-coupling was further reduced by about 1 Hz. The splittings at C-4 correspond well with those reported for **19** (J_{44} 164.7 Hz, J_{45} 5.4 Hz),[8] the relevant heteroatoms being quite distant. A J_{43} interaction (1.1 Hz) has also been found[8] in **19**; such a coupling was originally thought[6] to occur in **17**, however, in a later study[9] this weak splitting (1.0 Hz) was re-assessed as J_{45}. There was no indication of any J_{43} coupling in 1.

In the carbocyclic ring, C-5 showed second order character. In $CDCl_3$ a **doublet** of multiplets was observed, which at 90 MHz showed considerable fine structure with *ca*. 12 resolved lines in each branch. At low field in DMSO-d_6, multiplet fine structure was again seen, however, at high field the long range interactions were observed as a poorly resolved doublet of doublets, from which values of J_{57} and J_{54} were extracted (see Table 1). That the above fine splitting pattern was applicable was confirmed by the J_{55} interaction only obtained for **8**, and the **doublet** of doublets observed for **5** and **14**. The J_{55} coupling was slightly reduced when a *peri*-methyl group was present (*e.g.* 7 & 8) and also when *ortho* to a methyl group as in 7. The *peri*-coupling, J_{54} was of a similar magnitude to J_{45}; the *meta*-coupling, J_{57}, was slightly reduced across a 6-methyl substituent as in 7. The couplings were generally similar to those experienced[8] for **19**. The second order character of C-5 in $CDCl_3$ probably resulted from the minimal shift separation between H-5 and H-7 in this solvent ($\sigma_{5,7}$ = 0.049 p.p.m. in $CDCl_3$, but 0.157 p.p.m. in DMSO-d_6), see also later discussion.

Likewise C-6 showed first order character only at high field in DMSO-d_6, but was second order in $CDCl_3$. In the latter solvent the doublet branches each showed well defined, but different, splitting patterns (see Figure 1). The low field portion had the appearance of a doublet of doublets, with additional "wings". The high field portion was either a doublet of doublet type (15 MHz) or a triplet where the central peaks had merged, plus additional "wings" giving the appearance of a quintet (90 MHz). The overall line spacing of the



(a) (b) (c)

Figure 1

Signals in the ^{13}C proton coupled
N.M.R. spectrum of 1 in $CDCl_3$ at 90 MHz

(a)	C-6	:	downfield portion of doublet
(b)	C-6	:	upfield portion of doublet
(c)	C-10		

major components (ignoring the "wings") for both the low and high field portions was identical but frequency dependent, viz 8.3 Hz (15 MHz) and 9.4 Hz (90 MHz). In addition at each frequency the spittlings of the low field doublet of doublets were approx. 30% and 70% of the total width, consequently extraction of individual couplings was not possible. Similar splitting patterns were also observed for 2 at low field in $CDCl_3$. Since the respective portions were well resolved, they were accordingly treated as the X portion of an ABX spin system[20,21] to provide values of $(J_{AX} + J_{BX})(J_{66} + J_{68})$ at both frequencies. The results obtained (15 MHz : 171.4 Hz, 90 MHz : 170.9 Hz) were self consistent and in accordance with the calculated summation (169.9 Hz) from the first order splittings in DMSO-d_6. That couplings to only H-6 and H-8 were involved was confirmed by the clear J_{66} **doublets** observed for both **6** and 9, and was further supported by the well resolved quartet seen in 13. The couplings were thus very similar to those observed[8] for 19 (J_{66} 163.8 Hz, J_{68} 7.9 Hz). Since C-6 was overlapped in 3, 5 and **8** the effects of ortho-substitution or of an intermediate methyl group could not be reliably assessed.

It might have been expected that C-7 would exhibit only one long range ^3J interaction to H-5 and that the signal would thus appear as a simple **doublet** of doublets. This expected simple splitting pattern is supported by 3 in which an intense clear **doublet** only was seen with no indication of any further coupling, and further supported by **10** where C-7 was a well resolved quartet. The J_{77} coupling was reduced when ortho to **methyl** (e.g. **7** or **6**) and further diminished when adjacent to both (e.g. 13). The J_{75} coupling was reduced when an intermediate methyl group was present (e.g. 7, 13) and also diminished when ipso-substituted (e.g. 5,8).

Contrary to this simple expectation, C-7 consistently appeared as an 8-line pattern (see Table 1), which initially suggested a first order **doublet** of doublets of doublets with an additional weak ^2J coupling to H-6 or H-8. However, a detailed examination of each branch of the main ^1J **doublet** revealed that the individual fine splitting patterns appeared in distinctive pairs, which suggested that second order effects were operative such that the unexpected weakest splitting must instead be regarded as a "virtual" coupling.[22] Thus in $CDCl_3$ at both 15 and 90 MHz fine transitions 1 & 3 were better resolved compared with 2 & 4, whilst in DMSO-d_6 at both frequencies fine transitions 1 & 2 were more clearly defined than 3 & 4 (fine transitions numbered from low field to high field). Moreover, at 15 MHz in both solvents the fine splitting was 1.5 Hz, whereas at 90 MHz it was 2.0 Hz. Since the splitting was thus frequency dependent it cannot be considered as a true coupling and must therefore be regarded as a "virtual" interaction resulting from a second order effect. In contrast, the values of J_{77} and J_{75} remained essentially constant, save for any small digitisation effects (± 0.2 Hz), and were also very consistent with the values found for 2 (see Table 2), where such a "virtual" splitting was not encountered. A similar additional fine splitting has also been observed[23] in the spectrum of **18**. Since this too was found to be frequency dependent it has also been regarded as a "virtual" interaction rather than as a true J_{76} or J_{78} coupling. The other couplings at C-7 in 1 were broadly similar to those[8] in **19**.

In their excellent analysis of the ^{13}C proton coupled spectrum of coumarin (19), Chang et al.[8] also observed a doublet of doublets of doublets for C-7 and concluded that the finest 0.6 Hz splitting was to H-6 or H-8. Following on from this work; this might now also be envisaged as a similar "virtual" coupling. However, since the substituent effects of O in place of NH are known to be different and often result in enhanced couplings (see effects at C-2 and C-9 in this work), then the possibility that the fine coupling in **19** may not be "virtual" cannot be ruled out.

Unlike the other carbocyclic methine carbons, the signal for C-8 was always first order. The expected splitting interactions were confirmed by observation of a doublet only for 4 and 7 and also of a fine quartet only for 13. In 5 and 8, J_{88} was slightly reduced when ortho to a methyl group, with J_{86} diminished across the methyl group. The splittings at C-8 were generally similar to those[8] in **19**.

The $^3J_{CH}$ couplings at the carbocyclic ring carbons of 1, and certain related compounds are collected in Table 5. Hansen[2] has commented that the couplings at the β-carbons of bicyclic aromatic compounds, e.g. 20 are generally stronger than those at the α-carbons,

Table 5

Carbocyclic methine $^3J_{CH}$ coupling constants (Hz) in some aromatic and heteroaromatic compounds

Compound	20	18	19	1
(ref.)	(11)	(7)	(8)	(a)
α-carbons				
J_{57}	6.71 (b)	7.3	8.2	7.7 (d)
J_{86}		6.3	7.7	7.1
β-carbons				
J_{68}	8.43 (c)	8.6	7.7	7.9
J_{75}		8.5	8.9	8.5

(a) this work

(b) J_{13}

(c) J_{24}

(d) J_{57} reduced to 7.3 Hz only in 7.

a trend which has also been found to apply[7] in bicyclic heteroaromatic systems such as 18 and its derivatives. However, a different situation appears to hold in 19, since the reported[8] coupling constants instead may be seen to alternate around the ring, those ortho and para to the double bond being stronger than those ortho and para to the heteroatom. Inspection of Table 5 shows that the carbocyclic ring couplings in 1 correspond more closely with the revised trend now seen in 19. This would be even more obvious if the actual magnitude of J_{57} was slightly increased (this splitting was often unavailable due to second order effects) as the diminished value in 7 might suggest. Thus in benzenoid fused lactam/lactone systems such as 1 and 19 the respective magnitudes of the ^3J couplings at C-5 and C-6 are seen to be reversed compared to the fully aromatic systems.

Some comments on the second order effects experienced at certain carbocyclic ring methine carbons are now appropriate. Second order effects have been found to occur[20,21] in proton coupled ^{13}C N.M.R.spectra when the condition $0.5^1J_{CH} = \Delta\,\delta$ is satisfied (where $\Delta\,\delta$ = ^1H chemical shift separation between two closely closely protons associated with the adjacent carbon atom) such that there is then overlap of a ^{13}C satellite of one coupled proton at the ^1H chemical shift of the other. However, in the present work this condition is not met since there are no appropriate δ_{HH} separations at 360 MHz in the vicinity of 0.22 p.p.m. (80 - 82 Hz), see Table 4. The observed second order effects must therefore arise from the minimal chemical shift separations of the coupled protons, particularly with reference to the long range ^3J _meta_-interactions. Thus in $CDCl_3$ where H-5, H-7 & H-8 all absorb in a very narrow range (0.094 p.p.m.) the appropriate long range ^3J coupled carbons (_viz_ C-7, C-5 & C-6) all exhibit second order behaviour. In contrast, C-8 is first order since H-6 is reasonably well separated from the other carbocyclic ring protons. In this case $\Delta_{H-6,H-8}$ is 0.253 p.p.m. (91.1 Hz) which corresponds to a ratio of 1.116 which has been shown[20,21] to be too far removed from unity to lead to significant second order behaviour.

Analysis of the splittings at the quaternary bridgehead carbons C-9 (C-8a) and C-10 (C-4a) caused considerable difficulty since these low intensity signals were often broadened or unresolved. Use of methyl substituents as "blocking" groups subsequently permitted the coupling patterns to be ascertained.

The signal for C-9 generally appeared as a very broadened quartet with splittings of _ca_. 7 Hz (see Table 1), consistent with the anticipated[12] three ^3J couplings to H-4, H-5 and H-7. The spectrum of 15 was therefore examined, however, this compound is particularly insoluble. In our earlier study (in 9:1 DMSO-d_6 : $CDCl_3$)[15] of 15 C-9 was assigned at 139.0 δ. Slightly improved solubility has now been achieved using a mixed DMSO-d_6 : $CDCl_3$: acetone-d_6 solvent system, which allowed a very noisy proton coupled spectrum to be obtained that showed two discernible higher intensity signals at 161.7 δ and 141.0 δ. The former was C-2 (expect fine doublet, weak $^2J_{23}$ coupling), whilst the latter slightly stronger peak must be assigned as C-9, which should be a singlet (or possibly may be a fine doublet with a weak $^2J_{98}$ splitting). Hence the original 139.0 δ absorption must be re-assigned as C-7, the expected quartet splitting ($J_{7,Me-7}$) rendering this signal of such low intensity as to be indistinguishable from the noise. Our original assignments[15] of C-7 and C-9 in **15** therefore require reversal, such an error resulted because of the operation of the Me/Me peri-proximity effect,[24] the initial chemical shift estimations obtained by additivity of S.C.S. effects not being sufficiently reliable so as to produce an unambiguous assignment.

The coupling pattern at C-9 was subsequently deduced by reference to the spectra of **8** and **10** in which clearly resolved doublets were observed from which reliable values for J_{95} and J_{94} respectively were obtained. There was thus no indication of any weak $^2J_{98}$ coupling and hence C-9 in **15** must be regarded as a singlet. By reference to the spectra of other suitable compounds (see Table 2), further values of the splittings at C-9 were obtained, however, since each signal then appeared as either a doublet of doublets or triplet these values could be subject to possible digital error. The "through" ring[12] J_{95} was generally the strongest coupling, the magnitude being intermediate between that in **18** (6.4 Hz)[12] and in **19** (10.2 Hz)[8]. It would appear that replacement of the NH group in **1** by O in **19** results in variations in the C-9 couplings. Thus the lack of any $^2J_{98}$ interaction in **1** follows from the characteristic reduction of those ^2J couplings at carbons ortho to nitrogen, when compared to oxygen[8] (viz J_{23}(**19**) 4.5 Hz, J_{23}(**1**) 1.9 Hz, Δ 2.6 Hz ; J_{98}(**19**) 2.8 Hz, J_{98}(**1**) 0.0 Hz, Δ 2.8 Hz), a similar reduction being operative in each case. Likewise the reduction of the $^3J_{95}$ "through" ring coupling from 10.2

Hz in **19**,[8] to 7.9 Hz in **1** presumably results from a similar effect. The remaining splittings, viz the "through" ring J_{94} and the "cross" ring J_{97} appear to be quite similar in **1**, **18**[12] and **19**[8].

The other bridgehead nucleus, C-10, proved even more difficult to study, since this upfield carbon was often overlapped or obscured by other signals. Moreover, since 3-substituted 2-quinolones are less accessible,[18] the range of available compounds for study was more limited. Generally C-10 appeared as a complex or broadened triplet indicative of only two major couplings, however, in **13** a clear doublet was seen which would be consistent with the anticipated[12] three ^3J interactions. In **4**, C-10 showed multiplet character with a very wide unresolved central band, however, in **16** a well resolved doublet of doublets was observed. The splitting values obtained are expected to be representative since $^3J_{26}$ in both toluene and p-chlorotoluene are identical,[25] hence the effect of the meta-chloro substituent on the couplings appears to be negligible. The signal was overlapped with C-5 in **7**, however, with the methyl proton couplings specifically decoupled[7] the doublet of doublets was sufficiently accessible. Similar splitting patterns were also observed for **6** and **14**. The couplings at C-10 may therefore be summarised as $J_{10.3}$ 8.0 Hz, $J_{10.8}$ 4.9 Hz, these values being very similar to those in **18**[12] and **19**[8]; and $J_{10.6}$ 6.2 Hz, the smaller coupling being more consistent with **18**.[12] The change of heteroatom from O (in **19**) to NH (in **1**) therefore induced only minimal coupling variations when situated meta to the bridgehead carbon.

The C-10 signal was generally observed in **1** as a broadened triplet, however, at high field in $CDCl_3$ solution only, it instead appeared as a well resolved 13-line pattern with an approximate 2 Hz line separation (see Figure 1). The signal was initially thought to be first order, however, after assessment of the couplings from the "blocked" compounds study, it must be regarded as a second order multiplet. It may be described as comprised of a central triplet system (J 8 Hz) in which each line is further split inexplicably into an approximate 1:1:1 triplet with 2 Hz line separation, the above being superimposed upon a low intensity pattern with the appearance of a broadened quartet. Several other descriptions may also be devised.

The quaternary C-10 couples to H-3, H-6 and H-8, however, the peak separations between these protons (see Table 4) are too far removed from the appropriate 0.5^1J_{CH} values[20,21] to cause second order effects due to ^{13}C satellite overlap. It may be recalled that at 90 MHz in $CDCl_3$ solution, C-6 appeared as the X component of an ABX spin system ; it is therefore possible that the second order character is transmitted by mixing of the J_{68}, $J_{10,6}$ and $J_{10,8}$ interactions resulting in the observed additional multiplicity at C-10. A similar situation probably also operates in DMSO-d_6 , however, in this solvent C-10 is not so well resolved and only the very broadened major triplet is seen.

Although the C-9 and C-10 signals are very complex in the parent 1, an understanding of their interactions to assist in the assignment of very symmetrical derivatives can be of immense value. An example of the above will be published in due course.

Since methyl groups were used as "blocking" groups a study of the alkyl couplings has also been made, the results have been collected in Table 3. The ^1J couplings were generally close to 127 Hz whilst the ipso-methyl ^2J quartet interactions were invariably ca. 6 Hz and appeared to be independent of the position of substitution.[26] The ^3J couplings emanating from either the ring or methyl carbons were dependent upon the appropriate π-bond order[7] and were related to the appropriate ^3J vicinal coupling, through the previously established[14] relationship, $J_{CH/HH} \sim 0.6$. This relationship appeared to be more closely adhered to by the methyl carbon - ring proton splittings.

Table 6

Substituted 2-quinolones prepared from cinnamanilides

(A) **Substituted dimethylcinnamanilides**

$C_6H_5CH{=}CHCONHC_6H_3R_2$

R_2	m.p.	(lit.)	Elemental analysis Found (%) (a)		
			C	H	N
2,3-Me_2	192-4°	(183°)[29]	81.27	6.86	5.61
3,4-Me_2	175-6°		81.31	6.85	5.74
3,5-Me_2	137-8°		81.08	6.89	5.67
			(81.24)	(6.82)	(5.57)

(B) **Substituted dimethyl-2-quinolones**

Compound	m.p.	Elemental Analysis Found (%) (b)		
		C	H	N
10	268-9°	76.41	6.41	8.00
12	226-8°	76.45	6.48	7.97
14	206-7°	76.22	6.41	8.06
		(76.28)	(6.40)	(8.09)

(a) Calculated values for $C_{17}H_{17}NO$ shown in parentheses.

(b) Calculated values for $C_{11}H_{11}NO$ shown in parentheses.

A thorough study of the J_{CH} coupling interactions in a series of 2-quinolone derivatives has been presented, these appear to be generally intermediate between those previously observed for quinoline[7,12] and for coumarin.[8] Studies of the couplings in the 4-quinolone system and their relationship to those of chromone are in progress.

EXPERIMENTAL

4-Methyl substituted 2-quinolones 2,7-9 & 15 were obtained by the Knorr procedure as previously described.[27]

The remaining 2-quinolones were obtained from the appropriate cinnamanilides and aluminium chloride according to the general procedure of Johnson, Luker and Williams,[28] novel compounds so obtained are shown in Table 6. The spectrum of 3 was examined in admixture with 5.[17]

^{13}C N.M.R. proton coupled spectra were measured on a Jeol FX60 instrument in the "Gated-1" mode as previously described.[12]

The high field studies (360 MHz ^{1}H, 90 MHz ^{13}C proton coupled) were measured on a Bruker WH360 spectrometer at the University of Edinburgh, as previously described.[30]

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REFERENCES

1. Part 7, A. G. Osborne, Spectrosc. Letters, **11**, 351 (1978)
2. P. E. Hansen, Org. Magn. Reson., **12**, 109 (1979)
3. J. L. Marshall, "Carbon-Carbon and Carbon-Proton NMR Couplings : Applications to Organic Stereochemistry and Conformational Analysis", pp.42-64, Verlag Chemie International, Deerfield Beach, (1983)
4. S. R. Johns and R. I. Willing, Austral. J. Chem., **29**, 1617 (1976)

5. N. J. Cussans and T. N. Huckerby, Tetrahedron, 31, 2591 (1975)

6. Y. Takeuchi and N. Dennis, Org. Magn. Reson., 7, 244 (1975)

7. S. R. Johns, R. I. Willing, P. A. Claret and A. G. Osborne, Austral. J. Chem., 32, 761 (1979)

8. C.-j. Chang, H. G. Floss and W. Steck, J. Org. Chem., 42, 1337 (1977)

9. P. Ballesteros, R. M. Claramunt, T. Canada, C. Foces-Foces, F. H. Cano, J. Elguero and A. Fuchier, J. Chem. Soc., Perkin Trans. 2, 1215 (1990)

10. A. Yu. Denisov, V. I. Mamatyuk and O. P. Shkurko, Khim. Geterotsikl. Soedin., 948 (1984) ; 1223 (1984)

11. H. Seel, R. Aydin and H. Gunther, Z. Naturforsch., **33b**, 353 (1978)

12. A. G. Osborne and J. J. Hastings, Spectrochim. Acta, **47A**, 1583 (1991)

13. G. E. Jackson, W. E. Campbell and B. Davidowitz, Spectrosc. Letters, 23, 971 (1990)

14. P. A. Claret and A. G. Osborne, Org. Magn. Reson., 8, 147 (1976)

15. P. A. Claret and A. G. Osborne, Spectrosc. Letters, 9, 167 (1976)

16. A. G. Osborne, Tetrahedron, 39, 2831 (1983)

17. P. A. Claret and A. G. Osborne, Spectrosc. Letters, 10, 25 (1977)

18. R. Hayes, O. Meth-Cohn and B. Tarnowski, J. Chem. Res. (S), 414 (1980)

19. H. Sterk and H. Holzer, Org. Magn, Reson., 6, 133 (1974)

20. N. Cyr, R. G. S. Ritchie, T. M. Spotswood and A. S. Perlin, Canad. J. Spectrosc., 19, 190 (1974)

21. A. J. Jones, G. A. Jenkins and M. L. Heffernan, Austral. J. Chem., 33, 1275 (1980)

22. J. L. Musher and E. J. Corey, Tetrahedron, 18, 791 (1962)

23. A. G. Osborne, unpublished results.

24. A. G. Osborne, Magn. Reson. Chem., 27, 348 (1989)

25. M. J. Shapiro, J. Org. Chem., 43, 212 (1978)

26. T. A. Bryson, J. C. Wisowaty, R. B. Dunlap, R. R. Fisher and P. D. Ellis, J. Org. Chem., **39**, 1158 (1974)

27. P. A. Claret and A. G. Osborne, Spectrosc. Letters, **7**, 503 (1974))

28. K. M. Johnston, R. M. Luker and G. H. Williams, J. Chem. Soc., Perkin Trans. 1, 1648 (1972)

29. D. K. Chae, J. Korean Pharm. Soc., **21**, 173 (1977)

30. A. G. Osborne, R. Green, I. H. Sadler and D. Reed, Magn. Reson. Chem., **27**, 4 (1989)

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