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CARBON-13 NMR SPECTROSCOPY OF HETEROCYCLIC COMPOUNDS—III

A 20 MHz STUDY OF CHEMICAL SHIFTS AND CARBON-PROTON COUPLING CONSTANTS FOR THE METHYL COUMARINS

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Abstract—Complete assignments of chemical shifts and extensive assignments of carbon-proton coupling constants are presented for the 3-, 4-, 6-, 7- and 8-methylcoumarins, together with similar parameters for 5,8- and 6,8-dimethylcoumarin. Shifts in 6,8-dimethylcoumarin can be predicted with high precision from the substituent effects observed in the 6- and 8-methyl derivatives, and shifts are predicted for the 5-methyl derivative, which was not studied.

INTRODUCTION

With the exception of 5-methylcoumarin, the monomethylated derivatives of the 2 - *H* - 1 - benzopyran - 2 - one ring system are readily obtainable via syntheses which if not always high in yield are at least not long or complex in performance. They thus comprise accessible examples of this important class of compounds where virtually every proton in turn may be replaced by a simple substituent. Proton NMR spectra for these derivatives have recently[2] been discussed in considerable detail. In the preceding paper[3] we have described the spectral parameters for coumarin and some simple brominated derivatives. Here

Table 1.

	3-Methylcoumarin	4-Methylcoumarin		6-Methylcoumarin
	δ(CDCl$_3$)	δ(CDCl$_3$)	δ(DMSO)	δ(CDCl$_3$)
C_2	161.6 C_2CH_3 4.5 (a) - C_2H_4 11	159.4 - C_2H_3 4 -	159.3	159.9 - C_2H_3 4.5 C_2H_4 11.5
C_3	125.5 C_3CH_3 6.5 -	114.0 C_3CH_3 6 C_3H_3 170	114.2	115.5 - C_3H_3 171
C_4	138.8 C_4CH_3 5.5 C_4H_4 161 C_4H_5 5.5	151.4 not resolved from C_9	152.5 (d)	142.6 - C_4H_4 163 C_4H_5 5
C_5	126.7 - C_5H_4 4 C_5H_5 162 C_5H_7 7.5 (b)	123.9 - - C_5H_5 159 C_5H_7 6	124.8 (b)	127.0 C_5CH_3 5 C_5H_4 4 C_5H_5 159 C_5H_7 7
C_6	123.9$_5$ - C_6H_6 163 C_6H_8 7.5 (b)	123.4 - C_6H_6 164 C_6H_8 8	124.0	133.2 C_6CH_3 6 - C_6H_8 6
C_7	130.1 - - C_7H_5 7.5 - C_7H_7 162.5 (b)	130.8 - - C_7H_5 8 - C_7H_7 163	131.5 (b)	131.9 - C_7CH_3 5 C_7H_5 8 - C_7H_7 161
C_8	116.0 - - C_8H_6 7 - C_8H_8 164.5 (b)	115.8 - - C_8H_6 7.5 - C_8H_8 165	116.1 (b)	115.5 - - - C_8H_7 3 C_8H_8 168
C_9	153.0 (7.5, 7.5, 7.5)	152.6 not resolved from C_4	152.7	151.3 (8., 7., 3.)
C_{10}	119.3 (c)	119.0 (c)	119.3	117.7 (8., 5.) (b)
CH_3	16.7 C-H 129 CH_3-H_4 5	17.5 C-H 129 CH_3-H_3 5.5	17.7	19.8 C-H 127 CH_3-H_5 4 CH_3-H_7 4

Table 1 (*Contd*)

7-Methylcoumarin δ(CDCl$_3$)	8-Methylcoumarin δ(CDCl$_3$)	6,8-Dimethylcoumarin δ(CDCl$_3$)	5,8-Dimethylcoumarin δ(CDCl$_3$)
160.8 - C_2H_3 4.5 C_2H_4 11.5	159.9 - C_2H_3 4.5 C_2H_4 11.5	159.8 - C_2H_3 4.5 C_2H_4 11.5	159.7 - C_2H_3 4.5 C_2H_4 11
115.3 - C_3H_3 172	115.4 - C_3H_3 172 (b)	115.0 - C_3H_3 171.5 (b)	114.5 - C_3H_3 172 (b)
143.1 - C_4H_4 163 C_4H_5 4.5 (b)	143.1 - C_4H_4 163 C_4H_5 5 (b)	142.8 - C_4H_4 163 C_4H_5 5 (b)	139.8 - C_4H_4 161.5 - (b)
127.4 - C_5H_4 3.5 C_5H_5 161.5 -	125.0 - C_5H_4 4 C_5H_5 162.5 C_5H_7 8 (b)	124.6 - - C_5H_5 160 - (b)	132.8 C_5CH_3 5.5 C_5H_4 4 - C_5H_7 8.5 (b)
125.4 C_6CH_3 5 C_6H_6 161 C_6H_8 7	123.3 - C_6H_6 163 - (b)	132.6 C_6CH_3 5.5 - - (b)	124.4 $C_6(CH_3)_5$ 5 C_6H_6 160 - (b)
142.9 - C_7CH_3 7 C_7H_5 5 - -	132.4 - C_7CH_3 5 C_7H_5 8 C_7H_6 2 C_7H_7 160	133.3 $C_7(CH_3)_6$ 5 $C_7(CH_3)_8$ 5 C_7H_5 7.5 - C_7H_7 157.5	132.0 - $C_7(CH_3)_8$ 5 - - C_7H_7 159.5 (b)
116.8 C_8CH_3 5 C_8H_5 2 C_8H_6 5 - C_8H_8 161	125.2 C_8CH_3 6.5 - C_8H_6 6.5 - - (b)	124.6 $C_8(CH_3)_8$ 6 - - - - (b)	122.8 $C_8(CH_3)_8$ 6 - C_8H_6 6 - - (b)
154.0 (c)	151.6 (c)	149.6 (c)	152.0 (c)
116.3 (c)	117.8 (10., 7.5, 2.)	117.4 $C_{10}H_3$(7) 8 (b)	116.5 (c)
21.4 C-H 127 CH_3-H_6 4.5 CH_3-H_8 4.5	14.4 C-H 128.5 CH_3-H_7 5	19.6 (on C_6) C-H 127 CH_3-H_5 4 CH_3-H_7 4	17.0$_5$ (on C_5) C-H 127 CH_3-H_6 4.5
		14.1 (on C_8) C-H 128.5 CH_3-H_7 4.5	14.3 (on C_8) C-H 128 CH_3-H_7 4.5

(a) For each signal, chemical shifts are given in the top left corner. (For 4-methylcoumarin, shifts are also shown for a second solvent as indicated.) Values are quoted in p.p.m. from TMS as a secondary reference. Coupling constants are indicated by listing the nuclei involved, and all values are given in Hz. Unassigned values are shown in brackets.

(b) Broadened signals indicate the presence of unresolved coupling(s).

(c) Signals not well resolved from noise.

(d) Identifiable as C_4 because an incompletely resolved quartet structure could be seen.

we present shift and coupling data for the monomethyl coumarins (except the 5-substituted compound) which confirm the signal assignments proposed for coumarin. We also give details for two dimethylated molecules (5,8- and 6,8-dimethylcoumarin) which demonstrate that the methyl substituent effects obey quite precise rules. From these observations it is thus possible to predict the substituent chemical shifts for the 5-methyl group. This is of more than passing interest, since carbon shift data for the 6-methyl derivative have very recently been published[4] (with no details of assignments but in agreement with the results presented here) which were used in lieu of 5-methyl S.C.S. parameters in a study of the natural trisubstituted coumarin, siderin, which contains a 5-Me group.

RESULTS AND DISCUSSION

Carbon nuclei are numbered in the manner described previously.[3] The chemical shifts and ^{13}C-^{1}H coupling constants for the methyl and dimethyl derivatives are summarised in Table 1. Quaternary carbons could be distinguished as such by their smaller signal heights due to lack of nuclear Overhauser enhancements when spectra were obtained in a conventional proton noise decoupled mode of acquisition, and by the lack of a large one-bond C–H coupling constant on proton coupled spectra.

The carbonyl carbon, C_2, is readily distinguished by the very sharp lines, and characteristic couplings to H_3 and H_4 when present. The chemical shift range within which this signal falls is quite precisely defined (1·4 ppm) except in the case of 3-methyl coumarin where the band is perturbed slightly to low field and also exhibits a $^3J(C_2(CH_3)_3)$ coupling of 4·5 Hz. The signals for C_9 and C_{10} also fall within narrow ranges (2·7 and 3·0 ppm respectively) and may be assigned to these nuclei by a method analogous to that used for the brominated coumarins.[3]

With 3-methyl- and 4-methyl-coumarin the benzenoid carbon signals can easily be assigned as "alpha" and "beta" in position by off-resonance decoupling studies[5] and allotted to individual carbon atoms by comparison with the data for coumarin itself. With every derivative studied except for the 4-methyl case, C_5 is characterised by an inter-ring coupling of *ca.* 4 Hz with H_4. Table 2 shows the substituent chemical shifts induced upon replacement of the various protons in coumarin by a methyl group. As will be observed, the new quaternary carbons thus produced can be clearly identified because they show significant increases in chemical shift (of *ca.* 10 ppm in magnitude). On these quaternary signals a quartet coupling constant $^2J(C–CH_3)$ of 5–6 Hz is typically present, a quartet splitting $^3J(C–C–CH_3) \approx 5$ Hz also being produced at the carbons *ortho* to the site of substitution. The shifts of these *ortho* carbons in the benzenoid ring are only slightly displaced (−0·4 to +1·7 ppm) by the presence of the Me group; both these and the carbons *meta* to the substituent, also with small (−0·5 to +0·7 ppm) perturbations, show no consistent trends. The carbons *para* to a methyl do however show a consistent upfield movement of about 2 ppm. A combination of these substituent effects and the observation of couplings with the methyl protons makes the assignment of all the individual carbon signals a relatively easy process.

One-bond C–H couplings are quite significant. Those for C_3H_3 and C_4H_4 interactions are quite steady at about 172 and 163 Hz respectively, consistent with the values observed in coumarin. In the benzenoid ring these values again parallel their coumarin analogues with the notable exception that when a *meta* methyl substituent is present they drop quite consistently by *ca.* 3 Hz. The influence of a methyl on $^1J(CH)$ couplings for carbons *ortho* or *para* appears normally to be negligible in magnitude. With a methyl on C_8 a slight exception to the *ortho* effect may be noted, since $^1J(C_7H_7)$ is diminished by 3–4 Hz in 8-methylcoumarin and by about 6 Hz in 6,8-dimethylcoumarin.

In all cases where a proton is present *meta* to a benzenoid carbon the typically large $^3J(CH)$ coupling is present, while only isolated examples of ^2J or ^4J couplings always of low magnitude, may be seen. A three-bond coupling inter-ring from C_4 to H_5 with a magnitude of about 5 Hz is also characteristically seen on that carbon signal.

The substituent Me groups have chemical shifts which appear to be good indicators of their positions. For example, the three cases of an 8–Me group all fall in a range of 0·3 ppm at a distinctly lower field position than any other Me signals, while the two 6–Me values are only separated by 0·2 ppm and again fall in a specific region separated from other signals. Probably the only confusion to arise with Me signal assignments would be if 4- and 5-substituents were both present.

In Table 2 a comparison is made between the S.C.S. values predicted for 6,8-dimethylcoumarin by a combination of data for the 6- and 8-derivatives, and those actually observed. No value shows a discrepancy of greater than 0·25 ppm. The S.C.S. values predicted in Table 2 for a 5–Me group via data from 5,8-dimethylcoumarin are therefore given with a fair degree of confidence, and the influences indicated for all the benzenoid carbons are closely similar to those observed when the substituent is in other positions. Indeed, the data predicted for a 5–Me and observed for an 8–Me substituent compare extremely favourably.

EXPERIMENTAL

Carbon spectra were determined at 20 MHz as described previously.[3] $CDCl_3$ was employed as solvent and internal lock for all samples. Data for 4-methylcoumarin were also recorded in DMSO with 10% d_6-DMSO added for locking purposes. Spectra were referenced to the solvent carbon signal and shifts converted to δ values from TMS for presentation in the conventional manner. Coupling constants have been quoted to the nearest 0·5 Hz, and chemical shifts to the nearest 0·1 ppm.

3-Methylcoumarin. Reaction of the sodium salt of salicylal-

Table 2. Substituent chemical shift (S.C.S.) values for the methylcoumarins

	$3\text{-}CH_3$ (a)	$4\text{-}CH_3$	$6\text{-}CH_3$	$7\text{-}CH_3$	$8\text{-}CH_3$	Predicted 6,8-di-CH_3 (b)	Observed 6,8-di-CH_3	Observed 5,8-di-CH_3	Deduced 5-CH_3
C_2	+1.8	-0.4	+0.1	+1.0	+0.1	+0.2	0.0	-0.1	-0.2
C_3	+9.65	-1.85	-0.35	-0.55	-0.45	-0.8	-0.85	-1.35	-0.9
C_4	-6.0	+8.6	-0.2	+0.3	+0.3	+0.1	0.0	-3.0	-3.3
C_5	-0.7	-3.5	-0.4	0.0	-2.4	-2.8	-2.8	+5.4	+7.8
C_6	+0.15	-0.4	+9.45	+1.6	-0.5	+8.95	+8.8	+0.6	+1.1
C_7	-1.0	-0.3	+0.8	+11.8	+1.3	+2.1	+2.2	+0.9	-0.4
C_8	+0.15	-0.05	-0.35	+0.95	+9.35	+9.0	+8.75	+6.95	-2.4
C_9	-0.3	-0.7	-2.0	+0.7	-1.7	-3.7	-3.7	-1.3	+0.4
C_{10}	+1.1	+0.8	-C.5	-1.9	-0.4	-0.9	-0.8	-1.8	-1.4

(a) Substituent chemical shifts are shown as changes in chemical shifts, expressed in p.p.m. between coumarin (in $CDCl_3$ solvent) and the methyl derivative, also in $CDCl_3$.

(b) Values derived from the data for the 6- and 8-methyl derivatives.

dehyde with propionic anhydride at elevated temperature[6] gave the required product.

4-*Methylcoumarin*. This was synthesised from phenol and ethyl acetoacetate.[7]

6-*Methylcoumarin*. Condensation of malic acid with *p*-cresol in conc. H_2SO_4 gave the desired material.[8]

7-*Methylcoumarin*. *m*-Cresol and malic acid were reacted in the presence of $SnCl_4$ and the product extracted by steam distillation.[9]

8-*Methylcoumarin*. A reaction between *o*-cresol and malic acid under similar conditions yielded this derivative.[10]

6,8-*Dimethylcoumarin*. 2,4-Xylen-1-ol and malic acid were reacted in conc. H_2SO_4 and the product isolated by steam distillation.[11]

5,8-*Dimethylcoumarin*. 2,5-Xylen-1-ol gave the desired product under similar conditions to those employed above.[11]

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