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CARBON-13 NMR SPECTROSCOPY OF HETEROCYCLIC COMPOUNDS—II

A 20 MHz STUDY OF CHEMICAL SHIFTS AND CARBON-PROTON COUPLING CONSTANTS FOR COUMARIN AND SOME BROMOCOUMARINS

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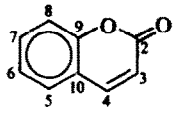
Abstract—Complete assignments of chemical shifts and extensive assignments of carbon-proton coupling constants are presented for coumarin through a study also involving detailed measurements on 3-bromo-, 6-bromo-, 7-bromo-, 3,6-dibromo- and 3,6,8-tribromo-coumarin.

INTRODUCTION

Coumarin is the simplest member of an important family of compounds all of which contain the 2-H-1-benzopyran-2-one ring system. There are many reports in the literature of proton NMR studies on coumarin derivatives, important recent examples being a complete iterative analysis of coumarin itself[2] and a nematic phase liquid crystal study of its molecular geometry.[3] Further sources are cited in a review[4] of proton NMR studies on simple heterocycles. On the contrary there is little[5-7] published information on *carbon* data for coumarin or its derivatives.

The aim of the work presented here and in subsequent papers is to make unambiguous assignments of carbon chemical shifts in a manner which relies only to a minimal extent on correlations with data derived from dissimilar structural systems since substituent-induced shifts obtained are not necessarily of comparable magnitudes. Much reliance has therefore been made on the *internal* consistency of shift changes following substitution, on the use of coupling constant data, and on the information obtained by performing single frequency off-resonance proton decoupling experiments. It has further been possible to elucidate substituent chemical shifts for this skeletal system which are used to predict both known and as yet unknown shift positions. In the discussion the carbon atoms in the basic coumarin skeleton are numbered as shown in 1.



1

RESULTS AND DISCUSSION

The carbon chemical shifts and ^{13}C–^{1}H coupling constants for coumarin and for five brominated derivatives are summarised in Table 1. Bromine was chosen as an initial substituent in this work since it is known[8,9] that its effect on the chemical shifts of aromatic carbon atoms is quite small even at the site of substitution. Thus the effect of such a substitution should be to cause a small perturbation in the carbon resonance position while leaving a signal which may be readily recognised by the loss of the nuclear Overhauser enhancement in a conventional proton-noise-decoupled spectrum. The structure of this signal on a proton coupled spectrum would again be characteristic since the large (160–180 Hz) one-bond ^{13}C–^{1}H coupling is lost, while long range interactions which have magnitudes characteristic of the number of bonds involved remain to yield diagnostic information.

The spectrum of coumarin at 20 MHz consists of eight lines. The line at highest field position (115·8, δ) is composed of two superimposed resonances (for C_3 and C_8) and partial separation of the coupled signals can be observed because the one-bond CH couplings and long range splittings are not identical. The intensities of three other signals are much reduced due to lack of nuclear Overhauser enhancement. These lines can be assigned readily to individual quaternary carbons in the following manner. That at the lowest field position (159·8 δ) is due to the lactone carbonyl carbon, C_2. The chemical shift is quite close to that observed[10] in unsaturated methyl esters. The fine structure observed on this signal in proton coupled spectra is also diagnostically useful. In all the compounds studied the lines are very sharp, and show couplings only to protons at C_3 and C_4. Typically the $^{3}J(C_2H_4)$ coupling is 11·5 Hz and is thus much larger than the $^{2}J(C_2H_3)$ interaction of 4·5 Hz. This relative order of magnitude is similar to that observed[11] for "Long-range" aromatic C–H couplings. When the 3-position is substituted by bromine, the remaining C_2H_4 coupling becomes slightly reduced in magnitude.

The other two low intensity signals, at 153·3 and 118·2 δ, may be assigned to C_9 and C_{10} respectively. Since the effect of the oxygen substituent –O–C(=O)–R is to shift the aromatic carbon to which it is attached downfield by *ca.* 23 ppm in a benzene system, and the influence of a vinyl group is much smaller,[8] the relative positions of these signals are adequately explained. Because of the inherently weaker signal strengths, fine structure for these resonances on proton coupled spectra could not always be resolved. However, in 3,6,8-tribromocoumarin the obser-

Table 1.

	Coumarin		3-bromocoumarin		6-bromocoumarin	
	$\delta(CDCl_3)$	δ(DMSO)	$\delta(CDCl_3)$		$\delta(CDCl_3)$	
C_2	159.8 (a)	159.6	156.3		159.4	
	C_2H_3	4.5	-		C_2H_3	4.5
	C_2H_4	11.5	C_2H_4	8.5	C_2H_4	11.5
C_3	115.8$_5$	115.9	111.0		117.5	
	C_3H_3	172	-		C_3H_3	172
	-		C_3H_4	5	C_3H_4	4
C_4	142.8	143.7	144.0		141.8	
	C_4H_4	164.5	C_4H_4	169	C_4H_4	164
	C_4H_5	5 (b)	C_4H_5	5	C_4H_5	4.5 (b)
C_5	127.4	128.1	126.9		129.9	
	C_5H_4	4	C_5H_4	4	C_5H_4	4.5
	C_5H_5	162.5	C_5H_5	164	C_5H_5	168
	C_5H_6	1	C_5H_6	1	-	
	C_5H_7	7.5	C_5H_7	8	C_5H_7	6
C_6	123.8	124.1	124.5		120.2	
	C_6H_6	164	C_6H_6	164	-	
	C_6H_8	7.5	C_6H_8	7.5	C_6H_8	6
C_7	131.1	131.5	131.6		134.2	
	C_7H_5	8.5	C_7H_5	8	C_7H_5	6.5
	C_7H_7	163.5	C_7H_7	164	C_7H_7	169.5
	C_7H_6 or C_7H_8	1	C_7H_6 or C_7H_8	1.5	-	
C_8	115.8$_5$	115.9	116.0		118.3	
	-		-		-	
	C_8H_6	7	C_8H_6	7	-	
	-		-		-	
	C_8H_8	164.5	C_8H_8	166	C_8H_8	167.5
C_9	153.3 (c)	153.4	152.6 (d)		152.7 (d)	
C_{10}	118.2 (c)	118.5	118.8		116.7	
			$C_{10}H_8$(?)	8	$C_{10}H_8$(?)	11
			(b)	(4.5, 1.)	(4., 3.)	

7-bromocoumarin $\delta(CDCl_3)$		3,6-dibromocoumarin δ(DMSO)		3,6,8-tribromo-coumarin δ(DMSO)	
159.4		155.7		154.9	
C_2H_3	4.5	-		-	
C_2H_4	11.5	C_2H_4	9.0	C_2H_4	9.5
116.6		112.0		112.7$_5$	
C_3H_3	172.5	-		-	
C_3H_4	1.5	C_3H_4	5	C_3H_4	4.5
142.4		143.5		143.1	
C_4H_4	164	C_4H_4	173.5	C_4H_4	174
(b)		C_4H_5	5	C_4H_5	5
128.6		129.5$_5$		129.2	
C_5H_4	4	C_5H_4	3.5	C_5H_4	4
C_5H_5	164.5	C_5H_5	171	C_5H_5	173
-		-		-	
-		C_5H_7	5.5	C_5H_7	6
127.6		120.9		121.6	
C_6H_6	170.5	-		Singlet	
C_6H_8	6	C_6H_8	5		
125.5		134.2		136.2	
(d)		C_7H_5	6.5	C_7H_5	6
-		C_7H_7	171	C_7H_7	174.5
-		-		-	

Table 1 (*Contd*)

119.6 - C_8H_6 3.5 - C_8H_8 171	118.2 - - (b) C_8H_8 169	116.4 C_8H_5 4 - C_8H_7 4 -
154.1 (d)	151.6 (d)	148.4 C_9H_4 9 C_9H_5 9 C_9H_7 7
117.6 (d)	116.3 $C_{10}H_8$(?) 11 (3.)	109.9 (4.5, 2., 2.)

a. For each signal, chemical shifts are given in the top left corner (for coumarin, shifts are also shown for a second solvent, as indicated). Values are quoted in p.p.m. from T.M.S. 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 an unresolved coupling.

c. Complex structure; not analysed.

d. Signals not well resolved from noise.

vation of three doublet couplings for C_9 with 9, 9 and 7 Hz magnitudes corresponds well with the fact that the C_9H_4, C_9H_5 and C_9H_7 interactions are all through three bonds. With C_{10} a coupling of *ca.* 10 Hz appears to be present except when C_8 is substituted, and therefore probably corresponds to $^3J(C_{10}H_8)$.

For coumarin, preliminary assignments for the remaining carbon nuclei were made with the aid of single frequency off-resonance decoupling experiments. When this decoupling frequency was centred at positions progressively sited from low to high field across the proton spectrum, the first multiplet to collapse completely to a singlet was that at 142·8 δ. Since the lowest field *proton* signal is known[2,12] to be H_4, this carbon must then be C_4. Conversely, one of the signals at 115·8$_5$ δ remained split when the others had all collapsed to singlets. This indicates the position of C_3, since H_3 is also known[2,12] to fall at the highest field position of all the coumarin proton resonances. The four remaining carbon signals could be classified quite readily as α (C_5, C_8) or β (C_6, C_7) in position by means of an extension (described in detail elsewhere[13]) to the method used[14] for similar assignments in *symmetrical ortho*-disubstituted benzenes or similar systems, whereby the band *shapes* produced in off-resonance decoupling experiments are absolutely characteristic of their substitution positions. Thus the second signal at 115·8$_5$ δ and that at 127·4 δ were classified as α, while those at 123·8 δ and 131·1 δ were assigned to the β environment.

It is possible to identify the α resonances in coumarin absolutely, because in all the compounds studied a ^3J inter-ring coupling of *ca.* 4 Hz was observed between C_3 and H_4. The $^1J(C_3H_3)$ interaction was noticably enhanced in all the compounds where C_6 bore a bromine substituent. Both C_5 and C_8 show the typically large ^3J coupling to a "*meta*" proton in the benzenoid ring[11] when that site (i.e. H_7, or H_6) is unsubstituted. Now, only the β signals remain to be identified absolutely. Application of the substituent effects observed in monosubstituted benzenes[8] suggests that C_7 would come at a slightly lower field position, but since the influences from groups at the ring junctions are *meta* and *para* in nature, such an assignment must be very tentative. An examination of the spectra for 6-bromo- and for 7-bromo-coumarin shows however that in each case only one signal, that for the halogen substituted carbon, is moved upfield, while the carbons *ortho* to the sites of substitution are in each case slightly displaced downfield. In the case of 7-bromocoumarin the substituent, and also the *o*-, *m*- and *p*-signal displacements are in fact remarkably similar to those observed between benzene and bromobenzene.[8] Data for 3,6-dibromo- and 3,6,8-tribromocoumarin confirm these findings and, together with parameters for 3-bromocoumarin (which are closely similar to those for coumarin, with C_3 again displaced upfield) allow tentative substituent effects for an 8-bromo group to be predicted. Although these data are derived from measurements in two solvent systems, it would appear from studies on coumarin that any solvent effects on chemical shifts are very small. The observed and predicted substituent chemical shifts in these brominated derivatives are summarised in Table 2. Carbons 6 and 7 also show the expected ^3J couplings to a proton when C_8 and C_5, respectively are unsubstituted. Their one-bond couplings again show significant increases (as already noted for C_5 and C_8) when an *ortho* bromine is present, the value for C_7H_7 in 3,6,8-tribromocoumarin being elevated by 11 Hz relative to that found for coumarin. In the tribromo derivative, the two and four bond CH couplings were also elevated to easily observable magnitudes.

Long range couplings involving the olefinic carbons can also be seen. In all the compounds studied except for coumarin itself, a $^2J(C_3H_4)$ splitting is observed although the reverse interaction, $^2J(C_4H_3)$ does not apparently seem to be present at measurable magnitude. Normally an inter ring coupling, $^3J(C_4H_5)$ of *ca.* 5 Hz may also be seen, similar to that found from C_5 to H_4.

It may be concluded in summary that assignments of carbon signals from coumarins can be made quite readily, with the aid of off resonance proton decoupled, and of

Table 2. Substituent chemical shifts (S.C.S.) (a)

	S.C.S. between coumarin and			Between 3,Br- and 3,6-diBr-coumarin	S.C.S. between coumarin and 3,6-dibromocoumarin		Between 3,6-dibromo- and 3,6,8-tribromo-coumarin (c)
	3-bromo-coumarin	6-bromo-coumarin	7-bromo-coumarin		Predicted (b)	Observed	
C_2	-3.5	-0.4	-0.4	-0.6	-3.9	-4.1	-0.8
C_3	-4.85	+1.65	+0.75	+1.0	-3.2	-3.85	+0.75
C_4	+1.2	-1.0	-0.4	-0.5	+0.2	+0.7	-0.4
C_5	-0.5	+2.5	+1.2	+2.65	+2.0	+2.15	-0.35
C_6	+0.5	-3.6	+3.8	-3.6	-3.1	-2.9	+0.7
C_7	+0.7	+3.1	-5.6	+2.6	+3.8	+3.1	+2.0
C_8	+0.15	+2.45	+3.95	+2.2	+2.6	+2.35	-1.8
C_9	-0.7	-0.6	+0.8	-1.0	-1.3	-1.7	-3.2
C_{10}	+0.6	-1.5	-0.6	-2.5	-0.9	-1.9	-6.4

a. All values are in p.p.m. and indicate the change in δ value upon substitution.

b. Obtained from the values for 3- and 6-bromocoumarin.

c. This effectively predicts the S.C.S. between coumarin and 8-bromocoumarin.

proton coupled spectra, the magnitudes of long range ^{13}C–^{1}H coupling constants being of particular value and significance.

EXPERIMENTAL

Carbon spectra were determined at 20 MHz using a Varian CFT-20 Fourier-Transform Spectrometer with 4 K data table for acquisition of free induction decays. For measurements on carbon-proton coupling constants, the coupling information was retained using a gated decoupling facility which permitted retention of the nuclear Overhauser enhancement. In order to maximise digital resolution for individual multiplets, coupled spectra were permitted to "fold", care being taken to minimise or avoid actual superposition of folded and non-folded resonances. For the measurement of coupling constants, line centres were visually estimated since the instrument peak listing procedure proved inadequate. Couplings are quoted to the nearest 0·5 Hz and chemical shifts to the nearest 0·1 ppm.

The spectra for coumarin, 3-bromo-, 6-bromo- and 7-bromo-coumarin were obtained from concentrated solutions in $CDCl_3$. Coumarin was also studied in DMSO (with 10% d_6-DMSO added as lock material) and this solvent was also employed for the measurements on 3,6-dibromo- and 3,6,8-tribromo-coumarin which were insufficiently soluble in chloroform. Spectra were referenced to the solvent signal, known separations from tetramethyl-silane being employed in order to present chemical shift data in the conventional manner. Concentrated solutions were used throughout in order to minimise spectral accumulation times. Solvent effects and concentration effects appeared to be of little importance.

Coumarin. A commercial sample was used without further purification.

3-Bromo-coumarin. This was prepared by room-temperature bromination of coumarin in carbon disulphide, followed by treatment of the intermediate with pyridine.[15]

6-Bromo-coumarin. Coumarin was nitrated, and then reduced to 6-amino coumarin, which was diazotized and reacted with Cu_2Br_2 using the method of Dey and Dalal.[16]

7-Bromo-coumarin. This derivative was obtained by reaction of *m*-bromophenol with malic acid as described by Rao and Sundaramurthy.[17] It was also synthesised by the addition of 7-hydroxycoumarin to triphenylphosphine dibromide[18] in acetonitrile followed by removal of solvent, heating to displace hydrogen bromide, and steam distillation.

3,6-Dibromocoumarin. This product was produced by the reaction of bromine with coumarin at 140° with carbon disulphide solvent in a sealed tube.[19]

3,6,8-Tribromocoumarin. The compound obtained from reaction of coumarin with mercuric acetate was treated with bromine to yield 3,6,8-tribromocoumarin.[20]

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