^{13}C Nuclear Magnetic Resonance Spectroscopy of 6- and 7-Substituted Coumarins. Correlation with Hammett Constants

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The ^{13}C n.m.r. spectra of coumarin and 19 6- and 7-substituted derivatives thereof have been obtained and fully assigned. The chemical shifts of the $\alpha\beta$-unsaturated lactone system have been correlated with Hammett constants: C-3 was found to fit very well with σ^+, and carbons 2 and 4 with σ. A satisfactory fit was found for the two ring-junction carbons with σ_p^+, but not with σ_m or σ_m^+. The electronic implications of these relationships are discussed.

IN connection with our interest in the chemical properties of naturally occurring coumarins, we have recently reported on the ^{1}H n.m.r. spectroscopy of synthetic 6- and 7-substituted analogues and the correlation of the H-3 and H-4 chemical shifts with Hammett constants.[1] In this paper we extend the investigation to the ^{13}C n.m.r. spectral data. Carbon shifts have certain advantages over their proton counterparts, namely their larger range of occurrence and their smaller dependence on medium effects. In addition, it is possible to observe non-protonated centres that are inaccessible by ^{1}H n.m.r. spectroscopy.
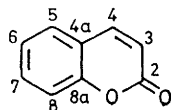
Since the early work on ^{13}C n.m.r. spectra of aromatic compounds, attempts have been made to correlate shift data to the Hammett equation.[2] It was noticed that for substituted benzenes, the *para*-carbon shift held a good linear relationship with σ_p^+, while for the *meta*-carbon the chemical shift was relatively invariant and without apparent regularity.[2] More recently such correlations have been successfully applied to side-chain carbons in disubstituted benzenes.[3,4] In particular, for substituted styrenes[4] it was shown that the presence of an electron-withdrawing group linked to C_β leads to an excellent fit between this carbon's shift and σ^+. For C_α, correlations were somewhat less successful. The coumarin system constitutes one more example in this series, with the advantage that the bicyclic structure eliminates the potential rotation of the olefinic moiety. In addition, the presence of a third carbon in the ' side-chain,' *i.e.* that of the carbonyl group may provide further information in the transmission of electronic effects along the π-system.

EXPERIMENTAL

The ^{13}C n.m.r. spectra were recorded on a Bruker WH–90 spectrometer operating at 22.63 MHz in the Fourier transform mode. Spectral widths of 4 200 Hz and the use of 4 K data points in the real spectrum resulted in a digital resolution of ± 0.05 p.p.m. All chemical shifts given in Table 1 are in p.p.m. downfield from internal SiMe$_4$, for solutions in 2 : 1 CDCl$_3$ + methanol, at normal probe temperature (*ca.*

30 °C). Concentrations of up to 1M were used when possible, although solubility was the limiting factor in many instances. The small influence of concentration differences was demonstrated by the minor (<0.2 p.p.m.) changes in a 0.3M spectrum of coumarin relative to 1M. Compounds soluble enough in CDCl$_3$ (coumarin and its methyl-, alkoxy-, acetoxy-, and chloro-derivatives) were also run in this solvent (see Results).

The samples were either commercially available, or were obtained by literature methods and have been previously characterized. They were not purified further.

The shift data in Table 1 were correlated to the Hammett equation (using the constants in Table 2) by means of a least-squares fit, with the aid of an IBM 360 computer. The slopes, intercepts and correlation constants thus obtained are presented in Table 3.

RESULTS

The chemical shift assignments in Table 1 are based on multiplicity in the single-frequency off-resonance decoupled (sford) spectrum, the use of established substituent parameters[2] and internal consistency. In many occasions, however, closely spaced signals could not be differentiated without the use of other coupling information.[5] The most commonly employed methods were specific decoupling of the very high field H-3[1] and the observation of lack of second-order coupling in the sford spectrum for methines without *ortho*-hydrogens (*i.e.* C-5 in the 6-substituted and C-8 in the 7-substituted series).[6] The spectra of some of the coumarins were recorded also in CDCl$_3$ as a solvent (see Experimental section). The shifts caused by addition of methanol to the medium turned out to be very constant and are as follows: C-2, 1.30 $\pm$ 0.10; C-3, -0.09 ± 0.08; C-4, 1.19 $\pm$ 0.14; C-4a, 5, 6, and 7, 0.58 $\pm$ 0.10; and C-8 and 8a, 0.27 $\pm$ 0.05 p.p.m. This pattern is strongly reminiscent, albeit in much reduced intensity, to the shifts observed by Sojka[7] in going to H$_2$SO$_4$ as a solvent and must, therefore, reflect the protonation of the carbonyl group by the alcoholic hydrogen. The consistency of these shifts allowed on occasion the confirmation of signal assignments.

Spectral data for the eight compounds † studied already reported in the literature,[7,8] is in good agreement with our results.

DISCUSSION

Correlation of Hammett Constants with the Ring-junction Carbon Shifts.—The two non-protonated centres of the

† Coumarin, 6-Me-, 7-Me-, 6-OH-, 7-OH-, 6-OMe-, 7-OMe-, and 6-Cl-coumarin.

TABLE 1

Carbon shifts of substituted coumarins

Subst.	C-2	C-3	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a
H	161.98	116.51	144.70	119.36	128.57	125.07	132.42	117.00	154.31
6-Me [a]	162.20	116.33	144.61	119.05	128.29	134.87	133.37	116.64	152.37
6-OH	162.75	116.51	144.66	119.86	112.79	154.41	120.72	117.91	147.88
6-OMe [b]	162.52	116.87	144.70	119.82	110.61	156.85	120.27	118.14	148.78
6-OAc [c]	161.66	117.37	143.98	119.77	120.77	147.24	125.98	118.09	151.73
6-NH₂	162.75	116.37	144.61	119.73	112.20	144.39	120.49	117.54	147.23
6-NO₂	160.03	118.82	143.39	119.45	124.39	144.57	127.02	118.41	157.90
6-CHO [d]	160.71	117.91	144.02	119.68	131.01	133.37	132.74	118.27	158.08
6-CO₂H [e]	161.21	117.28	144.30	118.95	130.65	127.79	133.55	117.28	157.00
6-CN [f]	160.21	118.73	143.16	120.86	133.33	108.94	135.37	118.73	156.85
6-Cl	161.47	117.87	143.66	120.59	127.89	130.42	132.37	118.68	152.86
7-Me [g]	162.43	115.28	144.84	117.10	128.34	126.34	143.93	117.19	154.50
7-OH	163.19	111.74	145.14	112.19	129.64	114.09	162.05	103.17	156.20
7-OMe [h]	162.70	112.79	144.93	113.11	129.61	113.24	163.61	101.14	156.22
7-OEt [i]	162.66	112.65	144.79	112.88	129.43	113.56	162.84	101.55	156.13
7-OAc [j]	161.66	115.96	144.16	117.23	129.34	119.05	153.77	110.70	154.90
7-NH₂	163.64	109.56	145.23	110.33	129.51	112.64	152.53	100.54	156.61
7-NO₂	160.06	120.08	142.65	124.11	129.50	119.53	148.17	112.73	154.12
7-CO₂H [e]	161.57	118.04	143.84	122.62	128.56	125.98	134.55	118.50	153.95
7-Cl	161.02	116.51	143.75	117.91	129.34	125.53	138.13	117.28	154.50

[a] δ(Me) = 20.67 p.p.m. [b] δ(OMe) = 56.08 p.p.m. [c] δ(OAc) = 20.99 and 170.81 p.p.m. [d] δ(CHO) = 191.12 p.p.m. [e] δ(CO₂H) = 167.69 p.p.m. [f] δ(CN) = 117.82 p.p.m. [g] δ(Me) = 21.71 p.p.m. [h] δ(OMe) = 56.03 p.p.m. [i] δ(OEt) = 14.64 and 64.60 p.p.m. [j] δ(OAc) = 21.08 and 169.60 p.p.m.

carbocycle, *i.e.* C-4a and C-8a, show a good correlation with σ_p^+ (not as good with σ_p, $\bar{r} \leqslant 0.91$) but practically none ($\bar{r} < 0.6$ and slopes of opposite signs for the two carbons) with σ^+ or σ, in parallel with previous reports.[2] In fact, the points for carbons with *meta*-substituents do not fall in the same general line as those with *para*-substituents, in contrast with the plots for the ' side-chain ' carbons (*vide infra*). Since the shift changes on *meta*-substitution are in every case of comparable magnitude (a 1.8—2.8 p.p.m. range), subtle non-electronic

TABLE 2

Hammett constants

Substituent	σ_m [a]	σ_m^+ [b]	σ_p [a]	σ_p^+ [b]
H	0	0	0	0
Me	−0.069	−0.066	−0.170	−0.311
OH	−0.002	d	−0.357	−0.92
OMe	0.115	0.047	−0.268	−0.778
OEt	0.150	d	−0.250	−0.812 [f]
OAc	0.390	0.25 [c]	0.310	−0.08 [c]
NH₂	−0.161	−0.16	−0.660	−1.3
NO₂	0.710	0.674	0.778	0.790
CHO	0.355	0.355 [e]	0.216	0.216 [e]
CO₂H	0.355	0.322	0.265	0.421
CN	0.678	0.562	0.660	0.659
Cl	0.373	0.399	0.227	0.114

[a] H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191. [b] Unless otherwise indicated, from H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979. [c] Ref. 4c. [d] Not available. [e] σ_m^+ and σ_p^+ taken to be identical to σ_m and σ_p, respectively. [f] K. V. Seshadri and R. Ganesan, *Tetrahedron*, 1972, **28**, 3827.

TABLE 3

Parameters of the significant lines $\delta = \rho\sigma + \delta_o$ obtained from the data in Tables 1 and 2

Carbon	Constants used	ρ	δ_o	$\bar{r}$ [a]	Number of points used
C-2	σ_m and σ_p	−2.6012	162.16	0.947	20
C-3	σ_m^+ and σ_p^+	4.6178	116.26	0.990	19
C-4	σ_m and σ_p	−1.6912	144.48	0.933	20
C-4a	σ_p^+	6.8348	118.65	0.985	10
C-8a	σ_p^+	5.7079	153.80	0.944	11

[a] Absolute values of the correlation coefficients.

influences on the chemical shift may have to be postul ated.

Correlation of Hammett Constants with the C-2 and C-4 Shifts.—In both cases there is a good correlation ($\bar{r} = 0.93$—0.95) with σ, the fit with σ^+ being poorer (see Table 3). As indicated in the previous section, taking of the *meta*- and *para*-substituted series separately leads to essentially the same results. The better agreement with σ than with σ^+ is explained by the lack of a direct resonance interaction between either carbon and any substituent in the benzene ring. Interestingly, the slope for the C-2 line is *ca.* 50% steeper than that of C-4, even though the latter carbon is fewer bonds away from the substituents. This may be due to the polarizibility of the C=O bond.

Correlation of Hammett Constants with the C-3 Shift.— This is the only carbon of the ' side-chain ' in direct resonance with the benzene ring, leading to a very large shift range (more than 10 p.p.m.). The correlation to σ^+ turns out to be excellent ($\bar{r} = 0.99$). This and the poorer fit with σ ($\bar{r} = 0.91$) are in agreement with the electron-withdrawing nature of the carbonyl group. Slightly larger deviations were observed for substituents that can hydrogen-bond, as related in other examples where non-protonic solvents were used,[4] in contrast to the usual aqueous conditions for the determination of σ^+ values. In the present case a proton source was present, but apparently differences in degree of hydrogen-bonding are still significant.

Conclusion.—The chemical shifts of the ' side-chain ' of the coumarin nucleus were successfully correlated with Hammett constants for carbocyclic ring substituents. The fact that the fit is as good as that of substituted styrenes [4] indicates that the interactions can be viewed as affecting a ' quasi-substituent ' CH=CH–CO₂R. In contrast, in a recent study of the bromination of benzo-furans, the transmission of substituent effects through both possible routes is shown to be of similar magnitude.[9]

Apparently, therefore, the presence of a carbonyl group effectively ' insulates ' the second potential interactive pathway in the coumarin system.

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