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Correlation of NMR Chemical Shifts of 2-Methyl Protons of Substituted Benzazoles with Hammett's Substituents Constants

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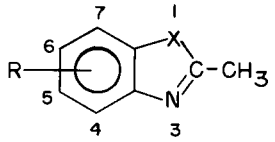
The chemical shifts of 2-methyl protons of twenty one 5- and 6- substituted benzazoles determined in carbon tetrachloride solution, were plotted against the Hammett substituent constants using σ_m for groups in the 5- position and σ_p for groups in the 6- position, obtaining satisfactory linear correlations. These results are taken to indicate that electronic effects are transmitted to the 2-position predominantly through the nitrogen atom and that virtually no transmission occurs through the hetero atom. The deshielding effect of the hetero atom is opposite to the electronegativity and this may be qualitatively explained in terms of different aromaticity of these heterocycles.

During our investigations on reactivity of 2-methyl groups in substituted benzothiazoles, used in the synthesis of polymethyne dyes, we correlated the reactivity of 2-methyl groups with pK_a values of related amines (1). The chemical shift values of methyl protons in position 2- in benzothiazole systems were recently used (2,3) to evaluate the reactivity of methyl groups; the chemical shift values were correlated with Hammett's σ_m constants for groups in the 5- position and σ_p constants for groups in the 6-position (I) thus obtaining a quite satisfactory linear relation. These results were taken to indicate that electronic effects are transmitted to the 2- site predominantly through the nitrogen atom.

H. H. Jaffè and H. Lloyd Jones (4) reported a detailed review on the application of the Hammett equation to heterocyclic compounds.

In the present work we measured chemical shifts of 2-methyl protons in substituted benzazoles (I) in order to extend our previous statements (2) to analogous systems containing a different hetero atom



X = Se,S,O.

R = See Table I.

(I)

(I, X = Se, O).

In Table I are listed chemical shifts, δ, of 2-methyl protons of the examined benzazoles and Hammett's σ constants (5) using in this case too, σ_m for R substituents in the 5- position and σ_p for R substituents in the 6- position.

The chemical shifts in Table I can be correlated with the Hammett's σ values by means of equations (1), (2), (3) which were derived from a least squares fit of the data.

(1) $\delta = 6.716\ \sigma + 167.79$ (I, X = Se)
(2) $\delta = 7.308\ \sigma + 166.34$ (I, X = S)
(3) $\delta = 6.823\ \sigma + 154.70$ (I, X = O)

In Fig. 1, Hammett's σ constants are plotted against δ values.

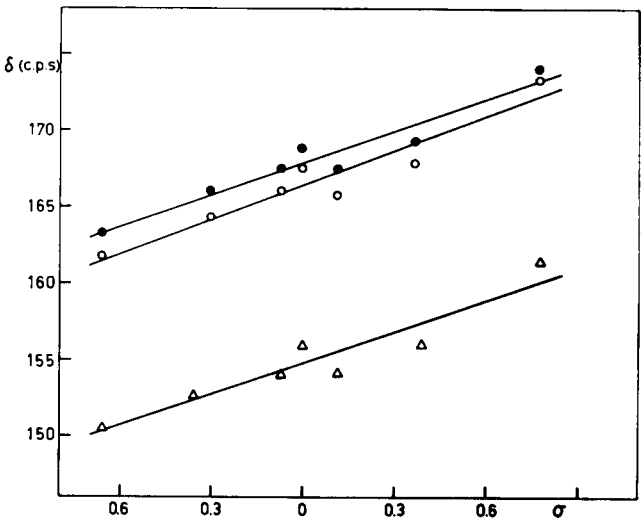


Fig. 1. Variation of 2-methyl protons δ values for substituted benzazoles with Hammett's σ constants.

(1) ●: form. (I), X = Se. (2) o: form. (I), X = S. (3) Δ: form. (I), X = O.

In Table II a set of data relative to equations (1), (2), (3) are reported.

Reported data suggest that the influence of substituents in the benzene ring on the shielding of 2-methyl protons, can be expressed in terms of Hammett's σ constants in benzoselenazoles and in benzoxazoles. These data provide evidence for a

TABLE I

Chemical Shifts of 2-Methyl Protons of Benzazoles in Carbon Tetrachloride Solution

Form. (I) X =	Substituent Form. (I), R =	Chemical shift δ (c.p.s.)	$\bar{\delta}$ (a)	σ (b)
	6-NO_2	173.820		0.778
	5-Cl	169.200		0.373
Se	5-OCH_3	167.460		0.115
(benzoselenazoles)	-H	168.780	168.021	0.000
	5-CH_3	167.520		-0.069
	5,6-CH_3	166.020		-0.303
	6-NH_2	163.350		-0.660
	6-NO_2	173.160		0.778
	5-Cl	167.760		0.373
S	5-OCH_3	165.720		0.115
(benzothiazoles)	-H	167.460	166.590	0.000
	5-CH_3	165.960		-0.069
	5,6-CH_3	164.310		-0.303
	6-NH_2	161.760		-0.660
	6-NO_2	161.340		0.778
	5-Br	155.910		0.391
O	5-OCH_3	154.080		0.115
(benzoxazoles)	-H	155.880	154.898	0.000
	5-CH_3	153.960		-0.069
	6-OH	152.640		-0.357
	6-NH_2	150.480		-0.660

(a) $\bar{\delta} = \frac{\Sigma\delta}{n}$; n = number of compounds for each series. (b) Values taken from: H. H. Jaffè (Ref. 5).

TABLE II

Set of Data Relative to Equations (1), (2), (3)

Equation n°	ρ (a)	r (b)	t (c)	S_δ (d)
(1)	6.716	0.958	7.52 (e)**	0.853
(2)	7.308	0.956	7.28 (e)**	0.960
(3)	6.823	0.936	5.94 (e)*	1.120

(a) Angular coefficients. (b) Correlation coefficients. (c) Student's t. (d) Standard error of the estimate. (e) One asterisk indicates "significant"; two asterisks "highly significant".

TABLE III

Preparation of Benzazoles

Benzoselenazoles R =	Ref.	Benzothiazoles R =	Ref.	Benzoxazoles R =	Ref.
6-NO_2	(a)	6-NO_2	(e)	6-NO_2	(j)
5-Cl	(b)	5-Cl	(f)	5-Br	(k)
5-OCH_3	(c)	5-OCH_3	(g)	5-OCH_3	(l)
-H	(d)	-H	(f)	-H	(m)
5-CH_3	(b)	5-CH_3	(h)	5-CH_3	(n)
5,6-CH_3	(b)	5,6-CH_3	(i)	6-OH	(o)
6-NH_2	(a)	6-NH_2	(e)	6-NH_2	(p)

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predominant transmission of electronic effects through the nitrogen atom, in all three series.

Calculations about the angular coefficients of the three lines of regression lead us to consider ρ_{Se}, ρ_S, ρ_O as essentially similar (6); this means that the susceptibility of the measurements to the effects of substituents in the three systems is nearly the same.

The hetero atom however plays an important role in establishing the shielding of 2-methyl protons, though it seems not to influence the transmission of electronic effects.

Mean values of δ (see Table I) are in the order $\bar{\delta}Se > \bar{\delta}S >> \bar{\delta}O$. Deshielding effects of the hetero atom is in the order Se>S>>O which is opposite to the electronegativity order. This is in agreement with values observed by P. Haake and W. B. Miller (7) in thiazoles and oxazoles. Thus we may suggest that, since oxygen is more electronegative than S and Se, the former is less prone than the latter to contribute to cyclic resonance in benzazoles. Benzoxazole is thus less aromatic than benzothiazole and benzoselenazole. The chemical shift values that we have found appear to be in agreement with this statement.

EXPERIMENTAL

Materials.

The investigated compounds were prepared and purified according to literature data reported in Table III.

N.M.R. Measurements.

Chemical shifts of 2-methyl protons were recorded on a Varian HA-100 spectrometer in 2.5% solution in carbon tetrachloride with tetramethylsilane (1%) as internal standard. Accuracy of measurements was estimated as ± 0.2 c.p.s.

Frequencies measured originally at 100 M c.p.s. have been multiplied by 3/5 to express all data for a 60 M c.p.s. oscillator.

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