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Nuclear Magnetic Resonance Spectra of Benzoxazole—an Analysis of a Five-spin System

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A five-spin iterative analysis was performed for the nuclear magnetic resonance spectrum of the benzoxazole protons. The converged values of the coupling constants showed that the long-range couplings between the oxazole ring proton and the other protons were supported by the McConnell's theory on the π-electron coupling in aromatic molecules using molecular orbital method, and the analyses for all combinations of the signs of the two prominent long-range coupling constants indicated that these were of the same sign. There was no distinct correlation between the chemical shifts of the protons and the calculated π-electron densities.

Introduction

Recently, the analyses of the complicated nuclear magnetic resonance (MNR) spectra of five-, six- or seven-spin systems have attracted the interests of many workers since the developments of refined numerical analysis methods and auxiliary experimental techniques have facilitated the perplexing complete analyses of such spectra as can not be readily interpreted in terms of the chemical formula and the low-order perturbation theory. In the work decribed here, a complete analysis of the five-spin system of the benzoxazole protons has been undertaken because the existence of long-range couplings between the oxazole ring proton and the others was revealed from the high resolution spectra which were measured in suitable solvents. The theoretical spectra which are calculated with the best fitting magnetic parameters showed good agreements with the experimental results. The chemical shift data reflected several interesting solvent effects, and the refined values of the coupling constants provided significant informations on the origins and strengths of the long-range couplings.

Experimental

The spectra were measured at 60MHz with a high resolution spectrometer type JNM-C-60H. The spectrum of each sample was recorded eight times with the alternations of high- and low-field sweeps, and the arithmetic mean of a line frequency relative to the internal reference signal of TMS was used for analysis. The solution in a 5 mm o.d. NMR sample tube was prepared to a concentration of 10 mole per cent and degassed by the repetitions of freezing in liquid nitrogen, pumping and thawing, then sealed under a high vacuum.

Analysis of Spectra

The analyses of the NMR spectra were performed with an iterative method developed by Swallen and Reilly.[2] Actual programmings and calculations were carried out using the Tokyo University HITAC 5020 Computer. The structural formula of the analyzed compound and the definitions used in designating the protons and coupling constants are shown in Figure 1.

A number of the spectra were measured under the changes of solvents in order to search a fully resolved spectrum, and the selected five spectra are illustrated in Figure 2.

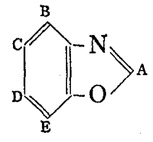

Fig. 1. The Structural Formula of the Analyzed Compound and the Notations used in Designating the Protcns and Coupling Constants

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[1] Location: *Oshika 160, Shizuoka.*

[2] J.D. Swallen and C.A. Reilly, *J. Chem. Phys.*, 37, 21 (1962).

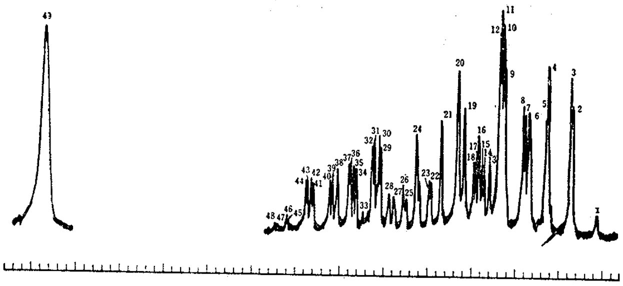

Fig. 2a. The NMR Spectrum of Benzoxazole measured in Methanol Solvent

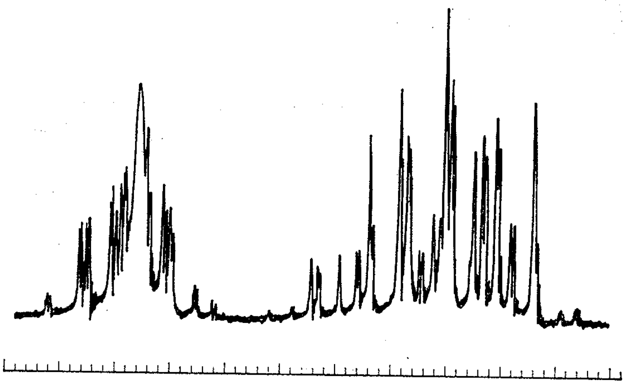

Fig. 2b. The NMR Spectrum of Benzoxazole measured in Toluene-d_8 Solvent

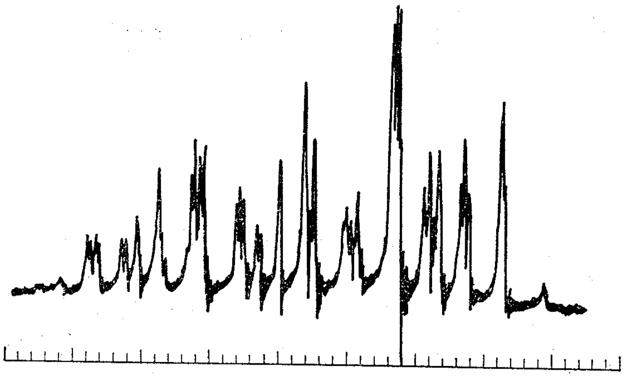

Fig. 2c. The NMR Spectrum of Benzoxazole measured in Acetone Solvent

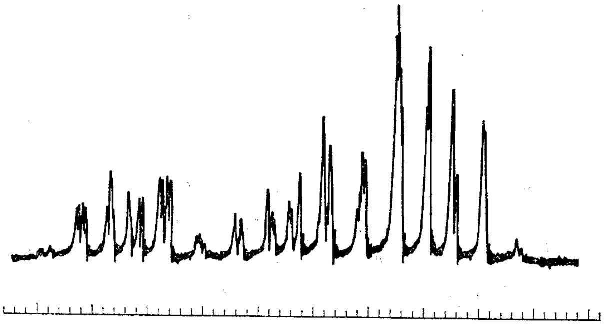

Fig. 2d. The NMR Spectrum of Benzoxazole measured in Pyridine-d_5 Solvent

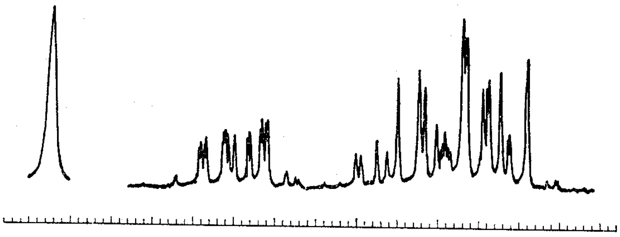

Fig. 2e. The NMR Spectrum of Benzoxazole measured in pure Liquid

These are all composed of a broad singlet of the A proton (1.2—1.5 cps half line-width), four groups of multiplets of the B, C, D, E protons and a few weak combination transition bands. The lowest-field multiplet and either of the higher-field two exhibit further slight splittings possibly due to long-range couplings with the A proton. The center of each multiplet shifts selectively depending on the nature of solvent, although there is an invariant tendency to the overlap of the two higher-field multiplets; in pyridine the two lower-field multiplets are most cleary differentiated from the others while only the lowest-field one is separated in toluene and in pure liquid of benzoxazole. In acetone and methanol, all the multiplets are rather uniformly separated but so close to each other as to provide the most complicated and resolved pattern. In toluene the signal of the A proton shows such a remarkable high-field shift that it appears just at the center of the lowest-multiplet so as to mask this widely while the resolution of the higher-field lines is much rised. The broad line-shape of the A proton signal may be possibly due to the interaction with the nitrogen quadrapole, and it is known from a preliminary calculation that this signal is a narrow multiplet over a range of 0.8 cps which is composed of 16 lines with almost equal intensity. The resolution of the A line with spin decoupling of the benzene ring proton resonance did not go on successfully.

As regards the assignments of the four multiplets to the four protons in the benzene ring, the lowest-field multiplet can be safely correlated with the B proton close to the nitrogen in reference with many similar examples in nitrogen-heterocyclic molecules which have been attributed to a low-field shift arised from the magnetic anisotropic effect of the neighbouring nitrogen. Then, the next lowest-field multiplet is necessarily assigned to the E proton because of the similar patterns of the two multiplets. Furthermore, this is confirmed by the fact that the proton chemical shifts of the A, C-disubstituted molecules are known to be downfield in a sequence of D<E<B.[3] It is difficult to differentiate the C and D multiplets becasue of only a slight difference below 2 cps between the resonance frequencies of the two protons. However, at the spectrum measured in toluene solvent are seen selective highfield shifts of either of the two multiplets and of the E multiplet. Accordingly, the former with a long-range coupling may well be assigned to the D proton closer to the E proton since such high field shifts as arised from the local diamagnetic field due to the anisotropic ring currents of the surrounding solvent molecules are likely to occur more similarly as the protons are closer to each other.

Before the final assignments of the absorption lines, the hypothetical resonance frequencies in the absence of long-range couplings were firstly obtained by removing the splittings with a first-order spectrum approximation, and then the four-spin iterative analyses of them were performed for the preliminary extraction of the chemical shifts and coupling constants except those connected to the A proton, which were used as initial parameter values in successive five-spin iterations. The results are shown in Table I.

TABLE I. The Converged Magnetic Parameters obtained by Four-spin Iterative Analyses

Solvent	h_B	h_C	h_D	h_E	J_{BC}	J_{BD}	J_{BE}	J_{CD}	J_{CE}	J_{DE}
Neat liquid	236.1	217.7	217.2	224.3	7.9	1.1	0.7	7.4	1.0	8.1
Acetone	236.9	224.0	224.7	231.8	8.1	0.9	0.6	7.3	1.4	8.0
Methanol	232.8	220.1	220.6	226.8	8.2	0.9	0.7	7.4	1.1	8.1
Toluene-d_8	230.8	211.9	211.2	217.7	8.1	1.0	0.8	7.4	1.1	8.0

All values are in cps. The magnetic screening contant h_i is equal to $\frac{\gamma H_0}{4\pi}(1-\sigma_i)\left(=\frac{\nu_i}{2}\right)$.

As these parameter values were of high approximate quantity, the convergence solutions of the secondary iterations could be obtained rather effectively. Making use of the informations obtained from the spectra, the initial values of the long-range coupling constants were chosen in a range which is shown as follows; $|J_{AB}|=0.1$—0.4 cps, $|J_{AC}|\simeq 0$ cps, $|J_{AD}|=0.2$—0.5 cps, $|J_{AE}|\simeq 0$ cps.

Iterative analyses of the spectra measured in methanol were performed with all combinations of the signs for J_{AB} and J_{AD}, and the unresolved signal of the A proton was also used for the least-squares determination of the experimental energy levels as follows; its peak frequency was assigned to the transitions of a few central lines of the A multiplet of which deviations from the observed peak were found to be less than 0.05 cps in a theoretical spectrum obtained in another independent iteration. Transitions corresponding to weak combination bands were not included in the equations giving energy level differences. These are as follows;

3→1; 12, 14, 15, 16→2; 7, 12, 13, 15, 16→3;
7, 10, 11, 13, 14, 16→4; 7, 8, 9, 13, 14, 15→5;
7, 8, 9, 10, 11, 12, 14→6; 19, 20, 22, 23, 24, 25, 26→7;
18, 21, 23, 24, 25, 26→8; 17, 18, 21, 22, 24, 25, 26→9
17, 20, 21, 22, 23, 25, 26→10; 17, 21, 22, 23, 24, 26→11;
17, 18, 20, 21, 22, 23, 24, 25→12;
17, 18, 19, 20, 26→13; 17, 18, 19, 20, 21, 26→14;
17, 18, 19, 20, 21, 24, 25→15;
17, 18, 19, 20, 21, 22, 23→16; 29, 30, 31→17;
28, 30, 31→18; 28, 29, 31→19; 27, 28, 29, 30→20;
27, 30, 31→21; 27, 29→22; 27, 28, 29→23;
27, 28, 31→24; 27, 28→25; 27, 28, 29, 31→26; 32→31

The 29→23 band (442—443 cps) was not distinct irrespective of 0.08—0.05 calculated intensity.

The least-squares solution of the energy levels[4] based upon the assignments corresponding to the combination of the signs $-+$ yielded the rms errors about ten times greater than those in the other combinations, and the successive itreration had to be abandoned. For other combinations of the signs $++$, $+-$, $--$, the least-squares determinations of the energy levels and successive iterations were found to be successful. The magnetic parameters which were converged below 0.001 cps and their errors are shown in Table II,

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[3] W. Brügel, "NMR Spectra and Chemical Structure," Academic Press, 1967.

[4] The energy level is numbered so as to increase as Iz descends and in a same Iz as an energy value decreases.

and the observed spectra and theoretical ones calculated with these converged parameters are shown in Table III.

Table II. The Converged Magnetic Parameters obtained by Five-spin Iterative Analysis

The relative signs of J_{AB} and J_{AD}	h_A	h_B	h_C	h_D	h_E	J_{AB}	J_{AC}
++	253.89 ±0.007	232.76 ±0.008	220.13 ±0.007	220.60 ±0.006	226.81 ±0.006	0.28 ±0.02	−0.02 ±0.02
−−	253.88 ±0.006	232.76 ±0.006	220.12 ±0.006	220.60 ±0.005	226.81 ±0.006	−0.27 ±0.03	0.00 ±0.02
+−	253.90 ±0.02	232.74 ±0.02	220.10 ±0.02	220.63 ±0.02	226.80 ±0.02	0.34 ±0.08	−0.04 ±0.07

The relative signs of J_{AB} and J_{AD}	J_{AD}	J_{AE}	J_{BC}	J_{BD}	J_{BE}	J_{CD}	J_{CE}	J_{DE}
++	0.37 ±0.02	0.01 ±0.02	8.18 ±0.02	0.88 ±0.02	0.72 ±0.02	7.36 ±0.02	1.09 ±0.02	8.14 ±0.02
−−	−0.35 ±0.02	−0.02 ±0.02	8.18 ±0.02	0.88 ±0.02	0.72 ±0.02	7.36 ±0.02	1.09 ±0.02	8.15 ±0.02
+−	−0.32 ±0.07	0.02 ±0.08	8.17 ±0.07	0.89 ±0.06	0.67 ±0.08	7.42 ±0.08	1.07 ±0.06	8.15 ±0.07

All values are in cps.

The magnetic screening parameter h_i is equal to $\frac{\gamma H_0}{4\pi}(1-\sigma_i)\left(=\frac{\nu_i}{2}\right)$.

The sign ± indicates a standard deviation error.

The relative intensities of the observed lines were not expressed in figures because the overlaps of lines prevented accurate measurements of line intensities. The theoretical spectrum obtained from the combination of the signs +− clearly shows a less agreement with the observed spectrum than the others at least with respect to line frequencies. Furthermore, the errors of the converged parameters are also greater in the sign +− than in the signs ++ and −−. A discrepancy on relative line intensities is that the calculated intensity of the 24 line which is unified by the overlaps of the 9→3, 23→14, 19→10 and 30→24 transition bands is 1.57 in the sign −+ and 1.98 in the signs +−, ++ and −−. The results obtained from the signs ++ and −− were in good agreements with the observations, but it is impossible to discern them without further informations. After all, it may well be said that the long-range coupling constants J_{AB} and J_{AD} are of the same sign, though the sign relative to the coupling constants connecting the benzene ring protons can not be determined.

Results and Discussion

Several noteworthy facts can be drawn from the present data; the E proton nearest to the oxygen is∼0.2 ppm downfield from the C, D protons in various solvents though a 0.05—0.1 ppm reverse difference is predicted at least by the π-electron densities calculated with the reasonable parameters[5] ($q_E>q_C>q_D\approx q_B>q_A$).

The B proton nearest to the nitrogen is affected least by solvent. The D proton becomes to be less shielded than the C proton only in polar solvents such as acetone or methanol. The order in J_{ortho} of J_{BC}, J_{DE} (8.1 cps)$>J_{CD}$ (7.4 cps) is in a good agreement with that of the corresponding π-bond orders ($P^{\pi}_{BC}=0.694$, $P^{\pi}_{DE}=0.684$, $P^{\pi}_{CD}=0.640$).

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5) A. Streitwieser, "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., 1961, Chapter 5.

TABLE III

Line	$J_{AB}+$, $J_{AD}+$				$J_{AB}-$, $J_{AD}-$			$J_{AB}+$, $J_{AD}-$		
	Obs. freq.	Transition	Calc. freq.	Calc. intensity	Transition	Calc. freq.	Calc. intensity	Transition	Calc. freq.	Calc. intensity
1	431.5	29 25	431.43	0.17	29 25	431.50	0.18	29 25	431.44	0.18
	431.5	18 11	431.49	0.18	18 11	431.43	0.17	18 11	431.34	0.17
2	434.9	32 30	434.92	1.03	27 19	434.92	1.03	27 19	434.93	1.04
	434.9	30 26	434.97	1.03	19 12	434.97	1.03	19 12	434.97	1.03
3	435.1	27 19	435.09	1.03	32 30	435.10	1.03	32 30	435.10	1.02
	435.1	19 12	435.10	1.02	30 26	435.11	1.02	30 26	435.10	1.02
4	438.2	24 16	438.24	1.44	24 16	438.28	1.44	24 16	438.27	1.43
	438.2	22 15	438.23	0.96	8 4	438.24	0.96	8 4	438.27	0.96
	438.2	10 5	438.27	1.44	10 5	438.23	1.44	10 5	438.19	1.45
5	438.5	8 4	438.51	0.97	22 15	438.50	0.97	22 15	438.51	0.96
6	440.8	28 22	440.77	1.32	28 22	440.82	1.33	28 22	440.79	1.33
	440.8	17 8	440.81	1.33	17 8	440.76	1.32	17 8	440.73	1.33
7	441.3	29 24	441.33	1.97	18 10	441.34	1.98	18 10	441.39	1.99
8	441.6	18 10	441.64	2.00	29 24	441.63	2.00	29 24	441.64	1.98
9	444.1	13 6	444.07	2.92	2 1	444.07	2.92	2 1	444.07	2.91
10	444.3	2 1	444.23	2.93	13 6	444.23	2.93	13 6	444.23	2.93
11	444.5	21 13	444.52	3.30	7 2	444.52	3.30	7 2	444.52	3.30
12	444.7	7 2	444.69	3.33	21 13	444.69	3.33	21 13	444.70	3.33
13	446.1	19 11	446.11	0.41	19 11	446.19	0.42	19 11	446.14	0.42
	446.1	30 25	446.19	0.42	30 25	446.12	0.41	30 25	446.06	0.41
14	446.9	22 14	446.98	0.53	8 3	446.98	0.53	8 3	446.97	0.54
15	447.1	8 3	447.16	0.56	22 14	447.16	0.56	22 14	447.10	0.57
16	447.7	23 15	447.64	0.77	23 15	447.67	0.75	23 15	447.68	0.75
	447.7	9 4	447.66	0.75	9 4	447.63	0.77	9 4	447.64	0.76
17	448.1	25 16	448.15	0.80	11 5	448.15	0.80	11 5	448.24	0.81
18	448.5	11 5	448.42	0.84	25 16	448.42	0.84	25 16	448.47	0.85
19	449.7	27 18	449.72	1.48	27 18	449.68	1.46	27 18	449.72	1.47
	449.7	32 29	449.68	1.46	32 29	449.72	1.48	32 29	449.72	1.48
20	450.6	28 21	450.57	2.07	28 21	450.61	2.09	28 21	450.57	2.09
	450.6	17 7	450.60	2.09	17 7	450.56	2.07	17 7	450.56	2.06
21	452.9	31 25	452.93	0.97	31 25	452.89	1.00	31 25	452.88	1.01
	452.9	20 11	452.88	1.00	20 11	452.93	0.97	20 11	452.94	0.98
22	454.3	22 13	454.32	0.67	8 2	454.32	0.67	8 2	454.35	0.66
23	454.5	8 2	454.49	0.65	22 13	454.49	0.65	22 13	454.47	0.64
24	456.3	30 24	456.10	0.40	30 24	456.26	0.41	30 24	456.26	0.39
	456.3	19 10	456.26	0.41	19 10	456.10	0.40	19 10	456.18	0.43
	456.3	23 14	456.39	0.60	23 14	456.33	0.58	23 14	456.27	0.59
	456.3	9 3	456.32	0.58	9 3	456.38	0.60	9 3	456.35	0.57
25	457.6	30 23	457.56	0.46	19 9	457.57	0.46	30 23	457.60	0.47
26	458.0	24 14	457.85	0.19	10 3	457.85	0.19	24 14	457.60	0.18
	458.0	19 9	457.94	0.46	24 14	458.01	0.20	19 9	457.83	0.44
	458.0	10 3	458.01	0.20	30 23	457.93	0.46	10 3	458.00	0.21
27	459.4	26 16	459.37	0.35	26 16	459.43	0.33	26 16	459.44	0.33
	459.4	12 5	459.43	0.33	12 5	459.37	0.35	12 5	459.41	0.35
28	460.2	15 6	460.16	0.44	15 6	460.22	0.42	15 6	460.19	0.41
	460.2	4 1	460.22	0.42	4 1	460.15	0.44	4 1	460.16	0.43
29	461.1	32 28	461.12	1.48	27 17	461.12	1.48	32 28	461.08	1.48
30	461.4	27 17	461.39	1.49	32 28	461.38	1.49	27 17	461.41	1.49
31	462.0	29 21	462.00	1.23	18 7	462.00	1.23	29 21	461.92	1.23
32	462.3	18 7	462.28	1.24	29 21	462.27	1.24	18 7	462.24	1.25
33	463.7	9 2	463.65	1.19	9 2	463.72	0.13	9 2	463.73	0.11
	463.7	23 13	463.73	0.13	23 13	463.66	0.12	23 13	463.64	0.13
34	464.3	31 23	464.30	0.92	20 9	464.31	0.92	31 23	464.42	0.89
35	464.7	20 9	464.71	0.90	31 23	464.70	0.90	20 9	464.64	0.92
36	465.2	24 13	465.19	0.73	10 2	465.19	0.73	24 13	464.97	0.75
37	465.4	10 2	465.33	0.77	24 13	465.33	0.77	10 2	465.38	0.77
38	467.0	30 22	466.97	0.72	30 22	467.10	0.73	30 22	466.77	0.72
	467.0	19 8	467.10	0.73	19 8	466.97	0.72	19 8	467.21	0.73
39	467.7	25 14	467.75	0.68	11 3	467.76	0.68	25 14	467.81	0.68
40	468.1	11 3	468.15	0.69	25 14	468.14	0.69	11 3	468.05	0.69
41	470.2	26 15	470.24	0.69	12 4	470.24	0.69	26 15	470.18	0.69
42	470.5	12 4	470.50	0.71	26 15	470.50	0.71	12 4	470.51	0.71
43	471.0	16 6	471.02	0.62	5 1	471.02	0.62	16 6	470.93	0.62
44	471.2	5 1	471.29	0.64	16 6	471.29	0.64	5 1	471.26	0.64
45	473.6	31 22	473.71	0.09	20 8	473.71	0.09	31 22	473.59	0.10
46	473.9	20 8	473.87	0.10	31 22	473.87	0.10	20 8	474.01	0.10
47	475.1	25 13	475.09	0.08	11 2	475.10	0.07	25 13	475.18	0.07
48	475.5	11 2	475.48	0.07	25 13	475.47	0.07	11 2	475.43	0.07

Comparison between the spectrum measured in methanol and the theoretical spectrum calculated with the converged magnetic parameters.

Absorption frequencies are all in cps.

The long-range couplings found here are undoubtedly π-electron transmitted couplings. According to the McConnell's theory[6] on the π-electron coupling in aromatic molecules using molecular orbital method, the π-contribution to the coupling between N and N′ protons is expressed as

$$(\beta Q)^2 P^2{}_{\mathrm{NN'}}/h\Delta E$$

Here, ΔE is the average electronic exitation energy, Q is the value of coupling constant and $P_{\mathrm{NN}}{}'$ corresponds to the ordinary bond order between carbon atom N and N′. A comparison between $|J_{\mathrm{obs.}}|$ and $P_{\mathrm{NN}}{}'$ is shown in Table IV.

Table IV. The Comparison between the Long-range Coupling Constants and the Corresponding π-bond Orders

	AB	AC	AD	AE
$\lvert J_{\mathrm{obs.}}\rvert$	0.27—0.28	0.00—0.02	0.35—0.37	0.01—0.02
$P_{\mathrm{calc.}}$	−0.192	0.033	0.178	−0.059

It is known that the above equation explains remarkably well the way by which the protons in benzoxazole are connected with long-range couplings.

The author wishes to thank Mr. S. Katayama for assistance in NMR measurements.

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[6] H. M. McConnell, *J. Chem. Phys.*, 24, 460 (1956).