A Note on the Proton Magnetic Resonance Spectra of Some Thiophene Derivatives*

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High resolution magnetic resonance spectra of the aromatic ring protons for a large number of substituted benzenes have at times been studied by several authors[1], but no available data were obtained for substituted thiophenes except for 2-bromo-5-chlorothiophene[2]. Here we present the experimental results and preliminary discussions on the proton magnetic resonance spectra of several thiophene derivatives. With respect to the number of the ring protons, they are less by two than the corresponding benzene derivatives, and so the spectra of mono-, di- and tri-substituted thiophenes are generally expected to show the structure of three quartets, two doublets and one singlet respectively. The analyses are simple for the ring protons of di- and tri-substituted thiophenes but more complicated for mono-substituted ones, and they will be discussed here qualitatively.

Experimental

The basic theory and experimental details of n-m-r measurements have been described by several authors in excellent articles, so they will not be given here.

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[1] P. L. Corio and B. P. Dailey, *J. Am. Chem. Soc.*, **78**, 3043 (1956); H. S. Gutowsky, D. W. McCall, B. R. McGarvey and H. L. Meyer, ibid., **74**, 4809 (1952); H. S. Gutowsky, C. H. Holm, A. Saika and G. A. Williams, ibid., **79**, 4596 (1957).

[2] W. A. Anderson, *Phys. Rev.*, **102**, 151 (1956).

TABLE I

Substituent	b. p. (°C)	Measured condition (Weight per cent)		
		Sample	CCl_4	C_6H_{12}
——		70.5		29.5
2-CH_3	107~112	95.9		4.1
3-CH_3	114~115	95		5
2, 3-$(CH_3)_2$	139~140	96.2		3.8
2, 4-$(CH_3)_2$	139~142	94.8		5.2
2-Cl		77.8		22.2
2-Br	148~151	81.0		19.0
2-I	72~74/15	82.5		17.5
2, 5-Cl_2		80.9		19.1
2, 5-Br_2		80.2		19.8
2, 5-I_2		26.5	67.2	6.3
2-Br, 3-CH_3	34.5~35.0/4.8	80.1		19.9
2-$COCH_3$	88/8	74.3		25.7
2-NO_2	m. p. 45~46	97		3
2-CHO	76/12	81.1		18.9
2-SO_2Cl	m. p. 32~33	93.2		6.8
2, 4-$(SO_2Cl)_2$	m. p. 76~77	8.3	89.9	1.8
2, 5-$(SO_2Cl)_2$	m. p. 44~45	28.8	68.3	2.9
2, 5-$(NO_2)_2$				
2-SO_2Cl, 3-CH_3	98~100/3	98.9		1.1
2-SO_2Cl, 5-CH_3		78.4		21.6
2, 4-$(SO_2Cl)_2$, 3-CH_3	m. p. 96	36.7	62.0	1.3
2, 5-$(SO_2Cl)_2$, 3-CH_3				

Materials.—All thiophene derivatives used in the present observations were synthesized by Y. M. and T. M., the details of the procedure will soon be published in the Journal of the Chemical Society of Japan, Ind. Chem. Sec..

Procedure and Apparatus. — The apparatus used in this research is a Bloch-type high resolution n-m-r spectrometer (Model V-4300B), purchased from Varian Associates, Palo Alto, California. Proton resonances were observed at a fixed frequency of 40 mc./sec. and the corresponding magnetic fields in the neighborhood of 9400 gauss.

The chemical shifts were read from the signals recorded with a Sanborn Model 127 Recorder, comparing with the shift of 227 cps for benzene-cyclohexane mixture, 1 : 1 by volume, as a reference, and the values given here are the averages, usually from about three recordings, and the small values were calibrated by running acetaldehyde, with its known splitting of 2.85 cps.

The values of chemical shift will not be sensitive to the presence of small amounts of impurities, especially in the case of C–H bonds, so that the samples were used after several times distillations or recrystallizations without any other special procedures of purification.

Samples which are solid at room temperature were measured in the super-cooled conditions after being heated above their melting points or dissolved in carbon tetrachloride. In such a case, it should be kept in mind that the occurrence of the additional shift due to the concentration effect or the molecular interaction is possible, so that the measured conditions are given in Table I.

Additional errors do not result from neglecting the bulk diamagnetic susceptibility corrections by using cyclohexane as a internal reference. Another error results from the difference of the reference concentration, but it is assumed that this error is small[3]. In some compounds, especially in 2-bromothiophene and in thiophene itself, it was observed that the line shapes were slightly changed with the variation of the concentration of the reference compound.

The results were reproducible within the deviation of about 4 cps.

Results and Discussion

Table of Chemical Shifts.—The chemical shifts of the ring protons obtained from the twenty-two compounds are given in Table II, in cps, indicating the separations from the cyclohexane signal, the larger value showing the lower field side. In the case where the signal is split by the indirect spin-spin interaction, the shift given here is that for the center of the resonance pattern. As for 2-methyl-, 3-methyl- and 2-bromothiophene, the assignments of their spectra are not given in Table II and they will be discussed in the latter paragraph of monosubstituted thiophenes.

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[3] P. L. Corio and B. P. Dailey, *J. Am. Chem. Soc.*, **78**, 3043 (1956); *J. Chem. Phys.*, **25**, 1291 (1956).

TABLE II

THE MAGNETIC RESONANCE DATA FOR THE RING PROTONS IN SUBSTITUTED THIOPHENES, REFERRED TO CYCLOHEXANE IN CPS, AT 40 mc./sec.

Substituent	Assignment				Mean shift	Mean shift from thiophene
	2-H	3-H	4-H	5-H		
——					220	0
2-CH_3	—				210	-10
3-CH_3		—			211	- 9
2, 3-$(CH_3)_2$	—	—	203	211	207	-13
2, 4-$(CH_3)_2$	—	197	—	197	197	-23
2-Cl	—	209	209	209	209	-11
2-Br	—				214	- 6
2-I	—	224	204	224	218	- 2
2, 5-Cl_2	—	204	204	—	204	-16
2, 5-Br_2	—	207	207	—	207	-13
2, 5-I_2	—	214	214	—	214	- 6
2-Br, 3-CH_3	—	—	204	219	211	- 9
2-$COCH_3$	—	248	223	248	239	19
2-NO_2	—	252	227	252	244	24
2-CHO	—	255	229	255	246	26
2-SO_2Cl	—	257	230	257	248	28
2, 4-$(SO_2Cl)_2$	—	266	—	281	273	53
2, 5-$(SO_2Cl)_2$	—	258	258	—	258	38
2, 5-$(NO_2)_2$	—	277	277	—	277	57
2-SO_2Cl, 3-CH_3	—	—	224	252	238	18
2-SO_2Cl, 5-CH_3	—	246	215	—	230	10
2, 4-$(SO_2Cl)_2$, 3-CH_3	—	—	—	288	288	68
2, 5-$(SO_2Cl)_2$, 3-CH_3	—	—	257	—	257	37

Indirect Spin-Spin Coupling Constants.—The indirect spin-spin coupling constants (J) for disubstituted thiophenes are given in Table III in cps, obtained by reading the scales of their spectra. In monosubstituted thiophenes, however, there are three independent coupling constants, the reasonable values of which can not be determined without theoretical calculations referring to the multiplet structure.

TABLE III

THE COUPLING CONSTANT (J) AND THE CHEMICAL SHIFT (δ) OF TWO RING PROTONS IN DISUBSTITUTED THIOPHENES IN CPS AT 40 mc./sec.

Substituent	J	δ
2, 3-$(CH_3)_2$	5.2	5.9
2-Br, 3-CH_3	5.6	14
2-SO_2Cl, 3-CH_3	5.5	27
2-SO_2Cl, 5-CH_3	4.1	31
2-Br, 5-Cl*	3.9	6.2
2, 4-$(SO_2Cl)_2$		15
2, 4-$(CH_3)_2$		$\simeq 0$
2, 5-Cl_2		0
2, 5-Br_2		0
2, 5-I_2		0
2, 5-$(NO_2)_2$		0
2, 5-$(SO_2Cl)_2$		0

* from Anderson's value[2].

The mean value (5.4 cps) of the indirect coupling constants between the 4- and 5-positioned protons (J_{45}) for three compounds, i.e. 2,3-dimethyl-, 2-bromo-3-methylthiophene and 3-methylthiophene-2-sulfonylchloride, is greater than the mean value of J_{34} (4.0 cps) for two compounds, 5-methylthiophene-2-sulfonylchloride and 2-bromo-5-chlorothiophene. The values of J_{35} can not be determined from the spectra of 2, 4-dimethylthiophene and 2, 4-thiophenedisulfonylchloride, for the signals of 3- and 5-positioned protons of these compounds are broad; perhaps they will have the unresolved multiplet structures.

With our results and the help of the values analyzed in detail for selenophene and furan[4], it can be assumed that $J_{45} \simeq J_{23} > J_{34} > J_{25} > J_{24} \simeq J_{35}$ in thiophene derivatives.

And also the methyl resonances for methylthiophenes have the fine structure due to spin-spin coupling with adjacent ring protons, having the approximate coupling constants of 1.0 cps, the signals of which are shown in b and d in Fig. 1.

Monosubstituted Thiophenes.—Nine compounds were measured and the spectra of

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[4] T. Isobe, Presented at the Symposium on the Structural Chemistry, held on Nov. 21, 1957, at Fukuoka.

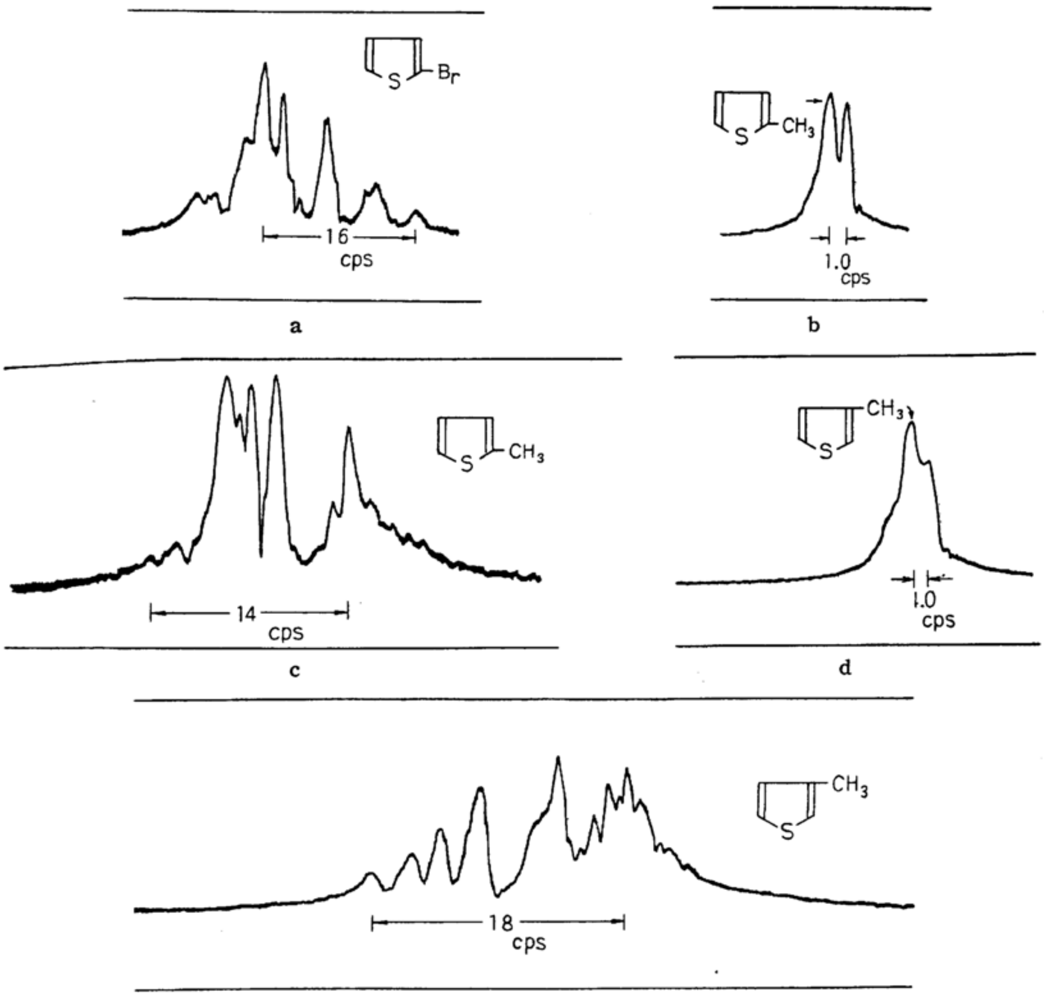


Fig. 1. The proton magnetic resonance spectra showing (a), 2-bromothiophene; (b), methyl group in 2-methylthiophene; (c), ring protons in 2-methylthiophene; (d), methyl group in 3-methylthiophene; (e) ring protons in 3-methylthiophene. Applied magnetic field increasing from left to right.

their ring protons can be classified into three types. The spectrum of 2-chlorothiophene is in the first type; it has a broad single line, so that the three protons in the ring are almost magnetically equivalent. The spectra of 2-bromo-, 2-methyl- and 3-methylthiophene are in the second type and they have the most complicated spectra as shown in a, c and e in Fig. 1, but their analyses are difficult for the present, so that they are not given in Table II. As for the others, 2-acetyl-, 2-iodo-, 2-nitrothiophene, 2-thiophenesulfonylchloride and 2-thiophenealdehyde, the spectra are in the third type and they are shown in a, b, c, d and e in Fig. 2. Their signals consist of two main parts separated approximately 20 cps or more. The intensity ratio of the high-field part to the low-field one is 1 : 2, corresponding to one proton and to two protons respectively. At the high-field side of the signal, there are three or four sub-lines. Therefore these sub-lines can be considered as the lines coming from the 4-positioned proton. At the low field side of their signal, there are two sub-lines and they can be assumed to be the lines coming from the 3- and 5-positioned protons, and that both protons have almost the same chemical shifts.

In the spectra of the ring protons in the third group, we can assume that J_{34} and J_{45} have approximately the same value of

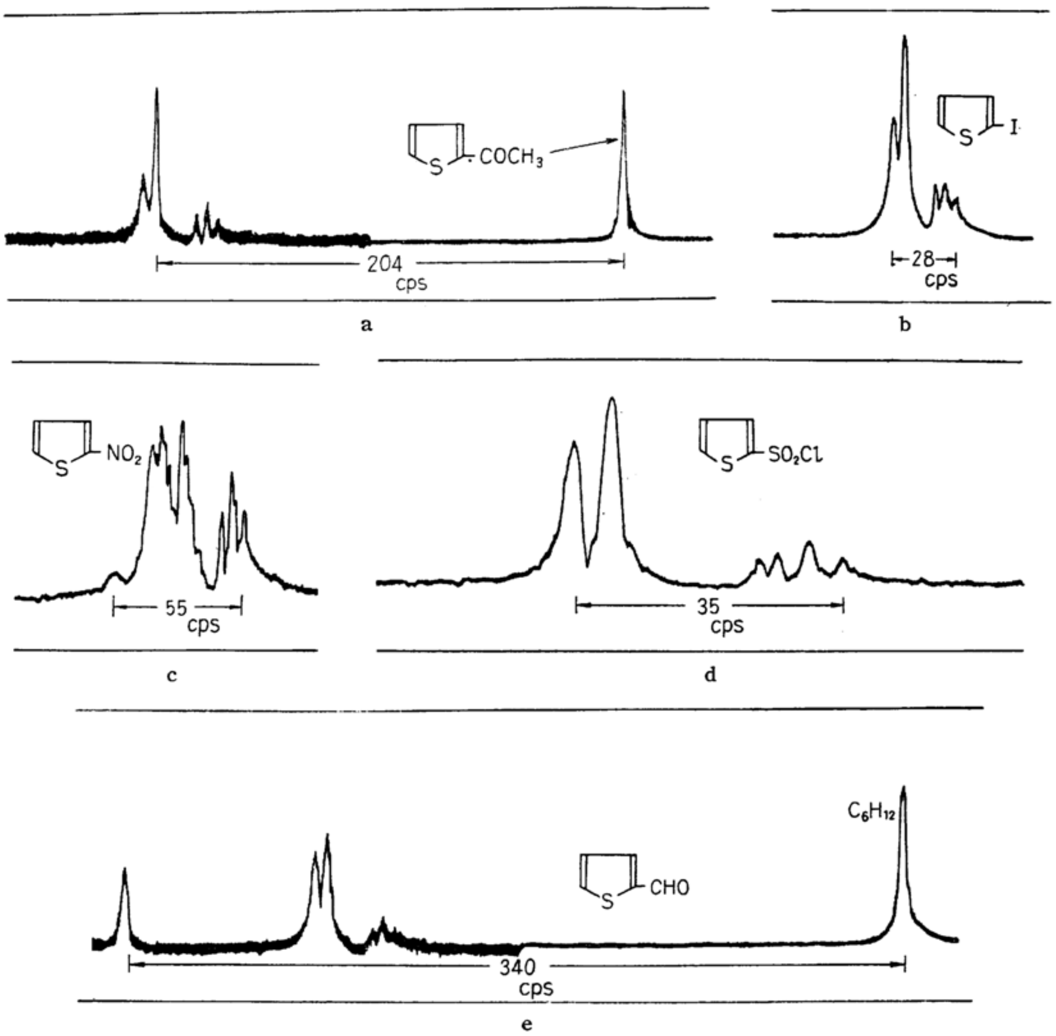
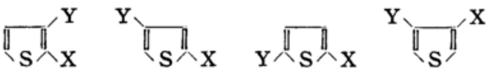


Fig. 2. The proton magnetic resonance spectra showing (a), 2-acetylthiophene; (b), 2-iodothiophene; (c), 2-nitrothiophene; (d), 2-thiophenesulfonylchloride; and (e), 2-thiophenealdehyde. Applied magnetic field increasing from left to right in all figures.

5 cps, closely consistent with the values shown in the preceding paragraph. The spectra of 2-nitrothiophene are more complicated than the others (Fig. 2 c), and in this figure, a signal which appeared at the lowest field side is assumed as coming from 2,5-dinitrothiophene by which the sample is contaminated.

In general, the multiplet structure of the n-m-r spectrum depends upon the ratio of the coupling constant to the chemical shift (J to δ). In monosubstituted thiophenes, it can be supposed that the chemical shifts are small as compared with the coupling constants in the first type, approximately the same in the second type and large in the third type.

Disubstituted Thiophenes. — The disubstituted thiophenes are the typical model of the two-proton system and there are four isomers as follows:



(I) (II) (III) (IV)

Their spectra consist of two doublets, but if X and Y are the same, the spectra for III and IV should have the single line.

The chemical shifts and coupling constants between the two ring protons are given in Table III; the samples in type IV were not measured. In the near future, we hope to obtain the measurements of this type for the determination of J_{25}, the coupling constant between the two protons by way of the sulfur atom.

Trisubstituted Thiophenes. — Two compounds were measured and they have a single line.

Substituent Effects to Thiophene Ring. —The nitro, sulfonylchloro, aldehyde and acetyl groups have the strong electron withdrawing power. The introductions of these substituents to the thiophene nuclei should have lessened the electron density of the ring protons, we can see these aspects in the experimental results shown in the seventh column of Table II. In the case of 2-nitrothiophene, the magnitudes of the shifts are large in 3- and 5-H but small in 4-H toward lower field. On the contrary, the shift of the ring proton to the lower frequency in the spectra of methylthiophenes is consistent with the effect of higher electron density in the ring due to methyl substitution.

Also in the halogeno-substituted thiophenes, the similar shifts toward the higher field were observed as shown in Table II. The I-effect of the halogen-substituent withdraws charge from the ring, while the E-effect donated charge to the ring. Therefore, the situation here shows probably a predominance of the E-effect over the I-effect.

It is hoped that the present results will be usefull in determining the structure of unknown thiophene derivatives and in analyzing the spectrum for thiophene in detail.

Summary

1) The chemical shifts of the ring protons for twenty-two kinds of thiophene derivative were measured, and the qualitative discussions on the substituent effects were also given.

2) The coupling constants between the ring protons for thiophene derivatives can be generally assumed to be $J_{45} \simeq J_{23} > J_{34} > J_{25} > J_{24} \simeq J_{35}$.

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