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The Substituent Effects in Thiophene Compounds. I. ^{1}H NMR and IR Studies in Methyl (Substituted 2-Thiophenecarboxylate)s

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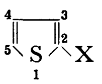
The ^{1}H NMR spectra and the IR carbonyl stretching frequencies of methyl (3-, 4-, and 5-substituted 2-thiophenecarboxylate)s have been reported. Good linear correlations between the chemical shifts of the ring protons in methyl (4- and 5-substituted 2-thiophenecarboxylate)s and those of the corresponding protons in substituted thiophenes were observed. The coupling constants in methyl (substituted 2-thiophenecarboxylate)s gave good correlations against the corresponding ones in substituted thiophenes. The IR carbonyl stretching frequencies in methyl (5-substituted 2-thiophenecarboxylate)s were correlated reasonably well with the chemical shifts of 5-protons in 2-substituted thiophenes. The coupling constants in methyl 2-thiophenecarboxylate series were found to vary linearly with the electronegativities of the substituents.

The ^{1}H NMR spectra have been obtained for 2- and 3-substituted thiophene,[1-3] and disubstituted thiophenes,[1,4] and the effects of the substituents have been discussed.

The present study was undertaken to examine the substituent effects in methyl (3-, 4-, and 5-substituted 2-thiophenecarboxylate)s in comparison with those of 2- and 3-substituted thiophenes. The correlations of the chemical shifts and of the coupling constants between methyl (substituted 2-thiophenecarboxylate)s and substituted thiophenes have been discussed in this paper. Attempts have also been made to compare the IR carbonyl stretching frequencies in methyl (substituted 2-thiophenecarboxylate)s with the chemical shifts in substituted thiophenes, and the coupling constants in methyl (substituted 2-thiophenecarboxylate)s with the electronegativities of the substituents.

Results and Discussion

The ^{1}H NMR spectra of 2- and 3-substituted thiophenes (**1** and **2**), and methyl (3-, 4-, and 5-substituted 2-thiophenecarboxylate)s (**3**—**5**) were measured in deuteriochloroform at 25 °C. The assignments of the signals were made tentatively on the basis of the chemical shifts and the coupling constants. The refined chemical



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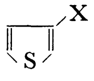

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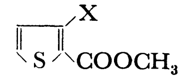

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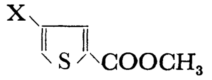

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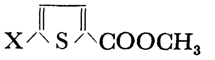

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Table 1. ^{1}H NMR chemical shifts(ppm) and coupling constants(Hz) for 2-substituted thiophenes

No.	X	δH_3	δH_4	δH_5	Others	J_{34}	J_{35}	J_{45}	Others
1	H	7.12	7.12	7.34	7.34 (H_2)	3.50	1.05	4.95	2.85(J_{25})
2	OCH_3	6.19	6.70	6.52	3.88 (OCH_3)	3.75	1.50	5.75	
3	CH_3	6.75	6.89	7.07	2.50 (CH_3)	3.35	1.20	5.15	1.10(J_{CH_3-3}) 0.30(J_{CH_3-4}) 0.15(J_{CH_3-5})
4	Cl	6.90	6.87	7.08		3.70	1.45	5.60	
5	Br	7.04	6.86	7.22		3.70	1.35	5.60	
6	I	7.24	6.80	7.35		3.60	1.20	5.45	
7	CHO	7.79	7.22	7.77	9.95 (CHO)	3.75	1.15	4.90	1.35(J_{CHO-5})
8	$COCH_3$	7.70	7.13	7.63	2.57 ($COCH_3$)	3.80	1.20	4.90	
9	$COOCH_3$	7.80	7.10	7.55	3.89 ($COOCH_3$)	3.70	1.30	5.00	
10	NO_2	7.93	7.08	7.56		4.00	1.60	5.30	

Table 2. ^{1}H NMR chemical shifts (ppm) and coupling constants (Hz) for 3-substituted thiophenes

No.	X	δH_2	δH_4	δH_5	Others	J_{24}	J_{25}	J_{45}	Others
1	H	7.34	7.12	7.34	7.12 (H_3)	1.05	2.85	4.95	3.50(J_{34})
2	OCH_3	6.24	6.74	7.17	3.81 (OCH_3)	1.60	3.10	5.20	
3	CH_3	6.88	6.89	7.20	2.27 (CH_3)	1.25	2.85	4.90	1.05(J_{CH_3-2}) 0.40(J_{CH_3-4}) 0.40(J_{CH_3-5})
4	Cl	7.10	6.96	7.27		1.35	3.30	5.10	
5	Br	7.23	7.02	7.27		1.30	3.15	5.00	
6	I	7.40	7.10	7.19		1.20	3.05	5.00	
7	CHO	8.12	7.55	7.38	9.94 (CHO)	1.20	2.85	5.10	0.35(J_{CHO-4}) 0.85(J_{CHO-5})
8	$COCH_3$	8.04	7.54	7.31	2.54 ($COCH_3$)	1.25	2.90	5.00	
9	$COOCH_3$	8.10	7.53	7.30	3.87 ($COOCH_3$)	1.15	3.05	5.05	
10	NO_2	8.31	7.66	7.37		1.40	3.35	5.30	

Table 3. ^1H NMR chemical shifts(ppm) and coupling constants(Hz) for methyl (3-substituted 2-thiophenecarboxylate)s

No.	X	δH_4	δH_5	$\delta COOCH_3$	Others	J_{45}	Others
1	H	7.10	7.55	3.89	7.80 (H_3)	5.00	3.70(J_{34}) 1.30(J_{35})
2	OCH_3	6.86	7.41	3.83	3.97 (OCH_3)	5.55	
3	CH_3	6.90	7.36	3.85	2.55 (CH_3)	5.00	0.40(J_{CH_3-4}) 0.40(J_{CH_3-5})
4	Cl	7.01	7.46	3.90		5.25	
5	Br	7.09	7.45	3.90		5.25	
6	I	7.22	7.43	3.90		5.10	
7	CHO	7.60	7.48	3.97	10.65 (CHO)	5.20	0.40(J_{CHO-4}) 0.80(J_{CHO-5})
8	$COCH_3$	7.47	7.14	3.90	2.59 ($COCH_3$)	5.10	
9	$COOCH_3$	7.45	7.28	3.91	3.89 ($COOCH_3$)	5.15	
10	NO_2	7.59	7.54	3.94		5.40	

Table 4. ^1H NMR chemical shifts (ppm) and coupling constants(Hz) for methyl (4-substituted 2-thiophenecarboxylate)s

No.	X	δH_3	δH_5	$\delta COOCH_3$	Others	J_{35}	Others
1	H	7.80	7.55	3.89	7.10 (H_4)	1.30	3.70(J_{34}) 5.00(J_{45})
2	OCH_3	7.42	6.50	3.86	3.80 (OCH_3)	1.85	
3	CH_3	7.60	7.12	3.86	2.27 (CH_3)	1.55	0.45(J_{CH_3-3}) 1.00(J_{CH_3-5})
4	Cl	7.63	7.32	3.89		1.60	
5	Br	7.68	7.44	3.89		1.50	
6	I	7.76	7.59	3.89		1.40	
7	CHO	8.17	8.27	3.92	9.91 (CHO)	1.40	0.30(J_{CHO-3})
8	$COCH_3$	8.17	8.20	3.91	2.54 ($COCH_3$)	1.45	
9	$COOCH_3$	8.16	8.25	3.90	3.88 ($COOCH_3$)	1.40	
10	NO_2	8.26	8.45	3.95		1.60	

Table 5. ^1H NMR chemical shifts(ppm) and coupling constants(Hz) for methyl (5-substituted 2-thiophenecarboxylate)s

No.	X	δH_3	δH_4	$\delta COOCH_3$	Others	J_{34}	Others
1	H	7.80	7.10	3.89	7.55 (H_5)	3.70	1.35(J_{35}) 5.00(J_{45})
2	OCH_3	7.53	6.22	3.83	3.94 (OCH_3)	4.20	
3	CH_3	7.61	6.75	3.85	2.51 (CH_3)	3.70	0.45(J_{CH_3-3}) 1.05(J_{CH_3-4})
4	Cl	7.58	6.92	3.87		4.05	
5	Br	7.54	7.06	3.87		4.00	
6	I	7.43	7.25	3.87		3.90	
7	CHO	7.83	7.73	3.94	9.97 (CHO)	3.90	0.15(J_{CHO-4})
8	$COCH_3$	7.76	7.63	3.92	2.59 ($COCH_3$)	4.00	
9	$COOCH_3$	7.73	7.73	3.91	3.91($COOCH_3$)	—	
10	NO_2	7.70	7.87	3.95		4.30	

Table 6. Frequencies(cm^{-1}) of C=O stretching vibration for methyl (substituted 2-thiophenecarboxylate)s

No.	X	Compound **3**		Compound **4**		Compound **5**	
		anti[a)]	*syn*[b)]	*anti*	*syn*	*anti*	*syn*
1	H		1722		1722		1722
2	OCH_3	1700	1724		1723	1709*	1717
3	CH_3	1711*	1720		1721		1720
4	Cl	1711	1733		1727	1718*	1726
5	Br	1711	1735		1729	1719*	1726
6	I	1711	1732		1725	1719*	1724
7	CHO	1725		1725	1735	1725*	1731
8	$COCH_3$	1727		1723	1730	1725*	1728
9	NO_2	1728	1745	1728	1739	1727*	1734

a) *anti-s-trans* form. b) *syn-s-trans* form. * Shoulder.

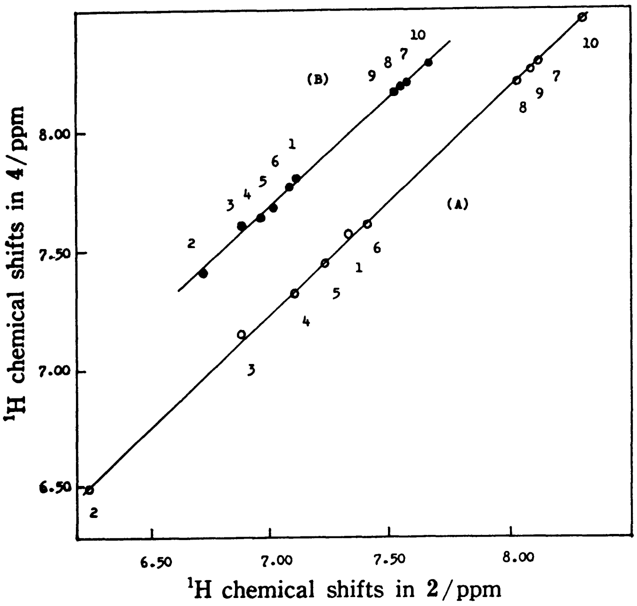


Fig. 1. Correlation between ^{1}H chemical shifts in **4** and **2**; numbering as in Table 2. A, $\delta_5(\mathbf{4})$ *vs.* $\delta_2(\mathbf{2})$; B, $\delta_3(\mathbf{4})$ *vs.* $\delta_4(\mathbf{2})$.

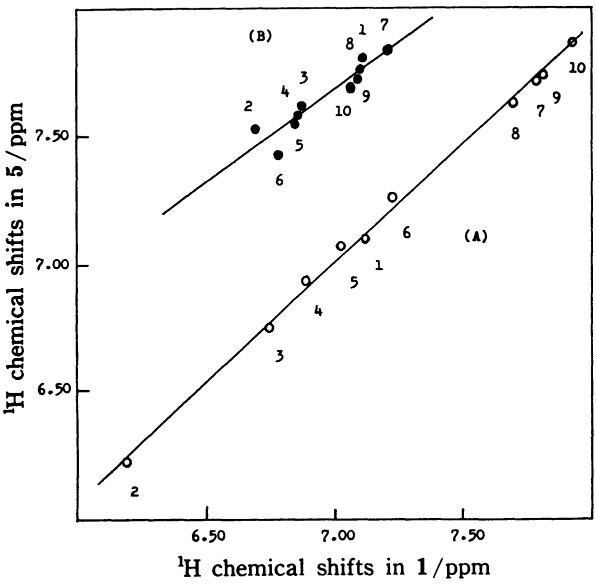


Fig. 2. Correlation between ^{1}H chemical shifts in **5** and **1**; numbering as in Table 1. A, $\delta_4(\mathbf{5})$ *vs.* $\delta_3(\mathbf{1})$. B, $\delta_3(\mathbf{5})$ *vs.* $\delta_4(\mathbf{1})$.

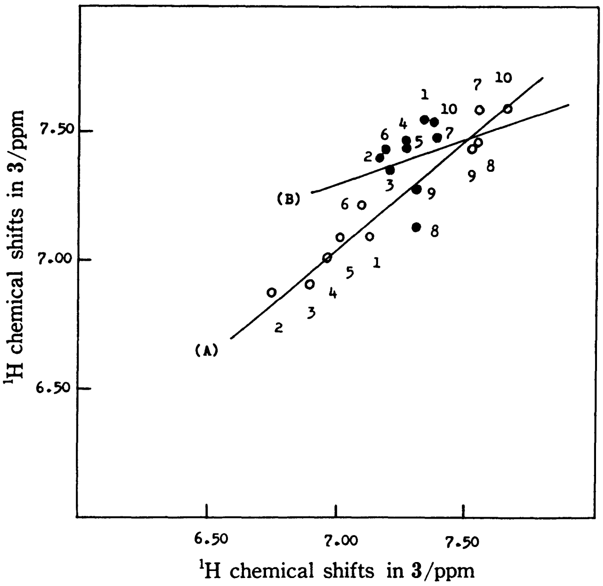


Fig. 3. Correlation between ^{1}H chemical shifts in **3** and **2**; numbering as in Table 2. A, $\delta_4(\mathbf{3})$ *vs.* $\delta_4(\mathbf{2})$; B, $\delta_5(\mathbf{3})$ *vs.* $\delta_5(\mathbf{2})$.

shifts and coupling constants were obtained iteratively using LAOCN 3.[5] The results are given in Tables 1—5. For convenience, the author uses, hereafter, the notation $H_r(\mathbf{N})$ for the *r*-th(position)-proton on the thiophene ring of the series of compounds **N**, $\delta_r(\mathbf{N})$ for its chemical shift, and *cc*, *p*, *i*, and *s* for the correlation coefficient, slope, intercept, and standard deviation in the least-squares analysis.

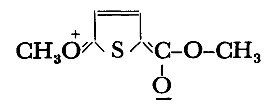
The $\delta_5(\mathbf{4})$ *vs.* $\delta_2(\mathbf{2})$ (A, *cc* 1.000, *p* 0.938, *i* 0.658, *s* 0.006) and the $\delta_3(\mathbf{4})$ *vs.* $\delta_4(\mathbf{2})$ (B, *cc* 0.999, *p* 0.907, *i* 1.323, *s* 0.013) plots gave excellent correlations, as shown in Fig. 1. Line A runs almost parallel with B. The correlation coefficient between $\delta_3(\mathbf{4})$ and $\delta_5(\mathbf{4})$ is 0.980, and this value is in accord with that between $\delta_2(\mathbf{2})$ and $\delta_4(\mathbf{2})$. These data show that the introduction of a methoxycarbonyl group into position 5 of 3-substituted thiophene is confined to the parallel transfer of the substituent effects on $H_2(\mathbf{2})$ and $H_4(\mathbf{2})$.

As seen in Fig. 2, good correlations were obtained with the $\delta_4(\mathbf{5})$ *vs.* $\delta_3(\mathbf{1})$ (A, *cc* 1.000, *p* 0.935, *i* 0.455, *s* 0.018) and $\delta_3(\mathbf{5})$ *vs.* $\delta_4(\mathbf{1})$ (B, *cc* 0.939, *p* 0.717, *i* 2.651, *s* 0.044) plots. The ratio of the slope of A against that of B is 0.768. Moreover, the slope of A is comparable with that of A in Fig. 1. The correlation coefficient and slope of the $\delta_4(\mathbf{5})$ *vs.* $\delta_5(\mathbf{4})$ plot are in good agreement with those between $\delta_3(\mathbf{1})$ *vs.* $\delta_2(\mathbf{2})$. These facts indicate that the methoxycarbonyl group in **5** reduces the substituent effect on the $\delta_3(\mathbf{5})$, whereas it has no effect on the $\delta_4(\mathbf{5})$.

Figure 3 shows good linearity (A, *cc* 0.982, *p* 0.835, *i* 1.207, *s* 0.051) between the effects of the substituents on $\delta_4(\mathbf{3})$ and those on $\delta_4(\mathbf{2})$, and no correlation (B, *cc* 0.215, *p* 0.357, *i* 4.806, s 0.115) between those on $\delta_5(\mathbf{3})$ and $\delta_5(\mathbf{2})$. The relationship between $\delta_4(\mathbf{3})$ and $\delta_3(\mathbf{4})$ was obtained as a linear response with a good correlation coefficient and unit slope. The correlation between $\delta_4(\mathbf{3})$ and $\delta_5(\mathbf{4})$ is almost equal to that between $\delta_4(\mathbf{2})$ and $\delta_2(\mathbf{2})$. However, apparently there is no correlation between $\delta_5(\mathbf{3})$ and $\delta_3(\mathbf{5})$, contrary to the situation between $\delta_5(\mathbf{2})$ and $\delta_4(\mathbf{1})$. Consequently, it seems that the chemical shift for the H_5 adjacent to the methoxycarbonyl group, which has a substituent on the *ortho* position, is affected considerably.

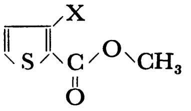
Methyl proton chemical shifts of methyl (substituted 2-thiophenecarboxylate)s, which are much less affected by the substituents on the ring, were found to have rather good correlations between proton chemical shifts of corresponding substituted thiophenes.

The chemical shifts of the ring protons of methyl (3-, 4-, and 5-substituted 2-thiophenecarboxylate)s were calculated by making use of the chemical shifts of the protons of 2- and 3-substituted thiophenes. The calculated chemical shifts are in good agreement with the observed ones, within 0.1 ppm in the series of compounds **4** and **5** (excluding δH_4 of methoxyl derivative). For example, the calculated ring proton chemical shifts were 7.64 and 7.31 ppm for methyl 4-chloro-2-thiophenecarboxylate (**4**, X=Cl) and 7.71 and 7.91 ppm for methyl 5-nitro-2-thiophenecarboxylate (**5**, $X=NO_2$). These calculated values were in good accord with the observed ones. In methyl 5-methoxy-2-thiophenecarboxylate, the contribution of the canonical structure **a** can be presumed to become larger. Therefore, δH_3 in the compound may be shifted to lower field.

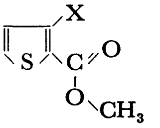


a

On the other hand, in the series of compounds **3**, there occur large deviations of the methoxyl, iodo, formyl, acetyl, and methoxycarbonyl derivatives. The two C=O stretching bands are observed in methyl 3-halo-2-thiophenecarboxylates (Table 6). These bands are considered to arise from the *syn-s-trans* and *anti-s-trans* forms as in *t*-butyl 3,4-dimethyl-2-thiophenecarboxylate.[6] Only one C=O band is observed and this is considered to be due to **b**-type isomer in methyl 2-thiophenecarboxylate. The field and magnetic anisotropy effects of the C=O function may be changed by the contribution of the **c**-type isomer. The field and magnetic effects of a halogen may be also affected by the repulsion of the lone pair electrons and the steric hindrance between the halogen and the methoxycarbonyl group. The δH_4 of methyl 3-iodo-2-thiophenecarboxylate, which is greatly influenced by the effects mentioned above, thus shifts to a lower field than that calculated by the contribution of this conformational change.

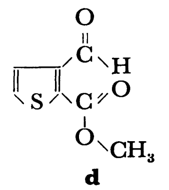


b

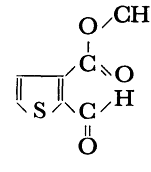


c

The ^1H NMR spectrum of methyl 3-formyl-2-thiophenecarboxylate was studied by Gronowitz and coworkers.[7,8] They have reported that aldehydic hydrogen resonance in this compound occurred at a field 0.54—0.65 ppm (depending on the solvents) lower than that of the unsubstituted 2-thiophenecarbaldehyde, but that the contribution to the chemical shift of intramolecular hydrogen bonding is small. However, judging from the following experimental results, it is considered that the contribution of the rotational isomer **d**, which is capable of forming intramolecular hydrogen bonding, is a better explanation of the results in methyl 3-formyl-2-thiophenecarboxylate. The resonance line of H_4 was found at 7.60 ppm, and that of H_5 at 7.48 ppm. The δH_4 was shifted towards a lower field than the values calculated, and the δH_5 towards a higher field. The chemical shift of the aldehydic hydrogen in 3-formyl derivative was 10.65 ppm, and shifted about 0.7 ppm lower than those in 4-, and 5-formyl derivatives. The chemical shift for methyl protons of methoxycarbonyl group is shifted lower than that of other compounds. The low field shift cannot be ascribed only to the effects of thiophene ring current and the substituent. The unusually low chemical shift of formyl proton might be due to the anisotropy effect of the ester carbonyl group located very close to it. If a weak hydrogen bond is persistent between the carbonyl oxygen and the formyl proton, the electric field effect lowers the chemical shift of formyl proton further. The strong ester carbonyl band in IR spectrum occurred at 1725 cm^{-1}, and could be assigned to *anti-s-trans* form **c**. The same consideration can be applied to methyl 2-formyl-3-thiophenecarboxylate. Its ^1H NMR spectrum exhibits the signals due to H_4 at 7.58 ppm, H_5 at 7.64 ppm, and the aldehydic proton at 10.62 ppm, indicating the presence of the preferred conformation **e**.

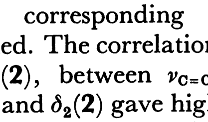


d

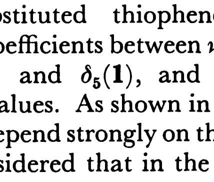


e

The chemical shifts for H_4 and H_5 in dimethyl 2,3-thiophenedicarboxylate are identical (7.51 ppm) in the calculations, but the two doublets occur at 7.45 and 7.28 ppm. Four planar conformations are considered in this ester. In methyl 3-thiophenecarboxylate, whose conformation study has not yet been reported, only one C=O stretching band is observed at 1726 cm^{-1}. It is considered that this compound exists in *syn-s-trans* form **f**, judging from the conformation of 3-thiophenecarbaldehyde.[9] From this consideration and a comparison with the chemical shifts of two ring protons in methyl 3-formyl-2-thiophenecarboxylate (conformation **d**) and methyl 2-formyl-3-thiophenecarboxylate (conformation **e**), the signal at higher field in dimethyl 2,3-thiophenedicarboxylate will be assigned to H_5, and that at lower field to H_4; the predominant conformation of this ester will lead to **g**. However, since the IR C=O stretching band occurs as a broad peak centered at 1734 cm^{-1}, other conformations are presumed to be present besides the **g** form.



f



g

The correlations between the C=O stretching frequencies (*syn-s-trans* form) of methyl (substituted 2-thiophenecarboxylate)s and the proton chemical shifts of the corresponding substituted thiophenes were examined. The correlation coefficients between $\nu_{C=O}(\mathbf{4})$[10] and $\delta_5(\mathbf{2})$, between $\nu_{C=O}(\mathbf{5})$ and $\delta_5(\mathbf{1})$, and between $\nu_{C=O}(\mathbf{3})$ and $\delta_2(\mathbf{2})$ gave high values. As shown in Table 6, $\nu_{C=O}(\mathbf{3})$, $\nu_{C=O}(\mathbf{4})$, and $\nu_{C=O}(\mathbf{5})$ depend strongly on the nature of the substituent. It is considered that in the series of **5** the substituent effect is mainly transmitted by the

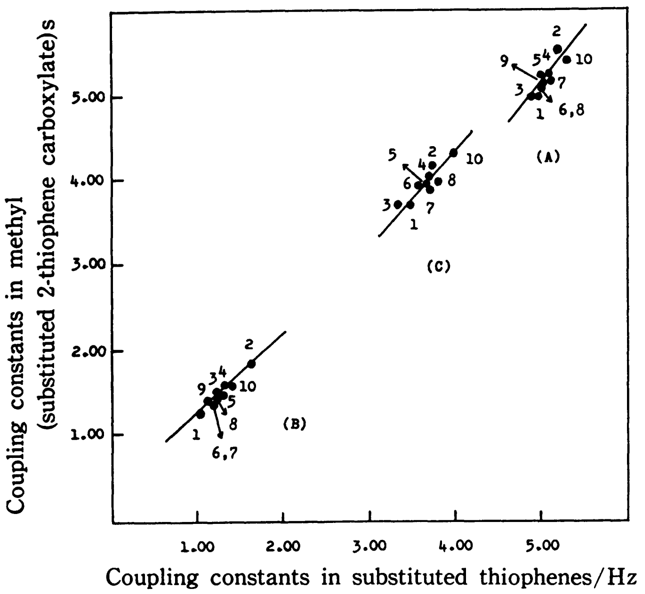


Fig. 4. Correlation between coupling constants in methyl (substituted 2-thiophenecarboxylate)s and substituted thiophenes, numbering as in Table 1. A, $J_{45}(\mathbf{3})$ *vs.* $J_{45}(\mathbf{2})$; B, $J_{35}(\mathbf{4})$ *vs.* $J_{24}(\mathbf{2})$; C, $J_{34}(\mathbf{5})$ *vs.* $J_{34}(\mathbf{1})$.

contribution of the canonical structure such as **a**, but in the series of **4** this occurs by the inductive effect. However, the correlation between $\nu_{C=O}(\mathbf{4})$ and $\nu_{C=O}(\mathbf{5})$ (*cc* 0.981, *p* 0.891) shows that the substituent effects on both frequencies have almost the same trend. It is interesting that the substituent effects in the series of **2** are almost insensitive to δH_5 but those in the series of **4** are transmitted strongly to the C=O stretching frequencies of the methoxycarbonyl groups. The slope between $\nu_{C=O}(\mathbf{4})$ and $\delta_5(\mathbf{2})$ is fivefold as steep to that between $\nu_{C=O}(\mathbf{5})$ and $\delta_5(\mathbf{1})$. The substituent effects on the C=O stretching frequencies in the series of **3**, which belong to *ortho* derivatives, are considered to become complicated due to the steric effect, in addition to the mesomeric and inductive effects, but show rather good correlations between $\delta_2(\mathbf{2})$.

The plots between the proton-proton coupling constants in methyl (substituted 2-thiophenecarboxylate)s and those in substituted thiophenes gave good correlations, as shown in Fig. 4. It is interesting that $J_{45}(\mathbf{3})$[11] gives a good correlation coefficient with $J_{45}(\mathbf{2})$ because $\delta_5(\mathbf{3})$ does not one with $\delta_5(\mathbf{2})$, in contrast to the good $\delta_4(\mathbf{3})$ *vs.* $\delta_4(\mathbf{2})$ correlation coefficient. The slopes of $J_{35}(\mathbf{4})$ *vs.* $J_{24}(\mathbf{2})$ and $J_{34}(\mathbf{5})$ *vs.* $J_{34}(\mathbf{1})$ plots are 1.00 and 0.97, respectively. This fact shows that the substituent effect is transferred equally, even though a methoxycarbonyl group is introduced into position 5 of **1** or **2**. However, the slope of $J_{45}(\mathbf{3})$ *vs.* $J_{45}(\mathbf{2})$ is 1.26, and the reason why the introduction of $COOCH_3$ into position 2 of **2** makes the substituent effect somewhat larger is not clear.

Studies on the relationships between the substituent electronegativity and the coupling constants in thiophene compounds have carried out by Bulman[12] and Galasso.[13] Bulman reported that the substituent electronegativity gave a good correlation with the sum of the coupling constants, but a rather more scattered one with the individual coupling constants in the series of compounds **1**. The relationship of the coupling constants in the series of compounds **3**, **4**, and **5** with the sum of the electronegativities of all substituents including methoxycarbonyl group was examined. Good correlations were found in all three cases. It is interesting that the three slopes are almost the same, even though the inductive and mesomeric effects of substituents on the spin-spin coupling are quite different in the three series.

Experimental

The ^1H NMR spectra of the compounds were obtained at 100 MHz on a JEOL PS-100 spectrometer. The chemical shifts were determined with an accuracy of ± 0.005 ppm relative to TMS as an internal standard and the coupling constants were determined with an accuracy of ± 0.02 Hz. The concentrations of solutions were adjusted approximately at 0.3 mol dm^{-3} with respect to substrates. The IR spectra were recorded on a Perkin–Elmer model 257 infrared spectrophotometer.

Most of materials used in this investigation were synthesized according to the methods reported,[14—25] or obtained by purification of commercially available materials.

Methyl 3-Chloro-2-thiophenecarboxylate. This material was prepared by the refluxing 3-chloro-2-thiophenecarboxylic acid[26] with methanol and H_2SO_4 for 4.5 h, mp 36 °C. Found: C, 40.92; H, 2.91; Cl, 20.07; S, 18.01%. Calcd for $C_6H_5ClO_2S$: C, 40.80; H, 2.85; Cl, 20.07; S, 18.15%. IR (KBr, cm^{-1}): 3110 (=C–H), 1719 (C=O), 1516, 1438, 1414, 730 (thiophene ring).

Methyl 3-Acetyl-2-thiophenecarboxylate. This material was prepared by the esterification of 3-acetyl-2-thiophenecarboxylic acid,[27] bp 103—105 °C/2.5 mmHg (1 mmHg≈133.322 Pa). Found: C, 52.02; H, 4.58; S, 17.67%. Calcd for $C_8H_8O_3S$: C, 52.16; H, 4.38; S, 17.41%. IR (neat, cm^{-1}): 3100 (=C–H); 1715, 1685 (C=O); 1510, 1438, 778 (thiophene ring).

Methyl 4-Chloro-2-thiophenecarboxylate. This material was prepared by the esterification of 4-chloro-2-thiophenecarboxylic acid,[28] bp 115—117 °C/21 mmHg. Found: C, 40.85; H, 2.78; Cl, 19.85; S, 18.28%. Calcd for $C_6H_5ClO_2S$: C, 40.80; H, 2.85; Cl, 20.07; S, 18.15%. IR (neat, cm^{-1}): 3130 (=C–H); 1718 (C=O); 1528, 1428, 1411, 749 (thiophene ring).

Methyl 4-Formyl-2-thiophenecarboxylate. This material was prepared by the esterification of 4-formyl-2-thiophenecarboxylic acid,[8] mp 63 °C. Found: C, 49.28; H, 3.63; S, 18.98%. Calcd for $C_7H_6O_3S$: C, 49.40; H, 3.55; S, 18.84%. IR (KBr, cm^{-1}): 3110, 3080 (=C–H); 1719, 1673 (C=O); 1535, 1454, 750 (thiophene ring).

Methyl 5-Methoxy-2-thiophenecarboxylate. This material was prepared by the esterification of 5-methoxy-2-thiophenecarboxylic acid,[14] mp 46 °C. Found: C, 48.98; H, 4.60; S, 18.76%. Calcd for $C_7H_8O_3S$: C, 48.82; H, 4.68; S, 18.62%. IR (KBr, cm^{-1}): 3080 (=C–H); 1699 (C=O); 1544, 1439, 1415, 748 (thiophene ring).

Methyl 4-Acetyl-2-thiophenecarboxylate. A solution of 4-acetyl-2-thiophenecarbaldehyde[29] (3.9 g, 0.025 mol) in ethanol (50 ml) was added to a shaken suspension of silver oxide, produced by adding NaOH (3.5 g) to $AgNO_3$ (9.0 g) in water (200 ml), and the mixture was shaken for 1 h. The free silver was removed by filtering, washed with water, and the filtrate was acidified with HCl. The white precipitate was recrystallized from water to give 4-acetyl-2-thiophenecarboxylic acid (3.2 g, 75%), mp 165 °C. The acid was esterified by refluxing with methanol and H_2SO_4 for 4.5 h to give methyl

4-acetyl-2-thiophenecarboxylate, mp 99—100 °C. Found: C, 52.37; H, 4.20; S, 17.51%. Calcd for $C_8H_8O_3S$: C, 52.16; H, 4.38; S, 17.41%. IR (KBr, cm^{-1}): 3110 (=C–H); 1709 (C=O); 1538, 1433, 751 (thiophene ring).

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10) The notation $\nu_{C=O}(\mathbf{N})$ is hereafter used for the carbonyl stretching frequency of the series of compounds **N**.

11) The notation $J_{rs}(\mathbf{N})$ is hereafter used for the spin-spin coupling constant between r- and s-protons on thiophene ring of the series of compounds **N**.

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